The American Journal of Surgery

PUBLISHED MONTHLY BY THE AMERICAN JOURNAL OF SURGERY, INC.
49 WEST 45TH STREET, NEW YORK, N. Y.

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NEW SERIES, VOLUME XLIII

JANUARY TO MARCH

1939

THE AMERICAN JOURNAL OF SURGERY, INC., PUBLISHERS
NEW YORK MCMXXXIX

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Printed in the United States of America

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EDITORIALS

RESOLUTION FOR 1939

WITH the start of a new year one cannot help but speculate regarding the prospects for the coming period. What have the next twelve months in store for medicine? Are we in for changes? And along what lines? Who will name them and control them?

To one who has been active in the ranks for over thirty years, a longing fills the heart for the old order of two decades or more ago when the primary thought in the minds of physicians was to care for the sick and advance the science of medicine. Perhaps the world has already moved to the point where change in administration has become inevitable, but we can hope that that primary aim will remain the central governing thought of the medical profession.

At any rate, we must assure ourselves that medicine will remain in the control of the physician. We must not be forced to transfer our professional birthright to politicians, to large foundations or to physicians who have never devoted ten minutes to the actual practice of medicine. We know that we must meet the economic needs of the times, and, after due and deliberate study and discussion, we shall do so. But we must also stand shoulder to shoulder, yielding no infinitesimal part of our heritage, allowing no outsiders to regulate and control our profession.

Are we to have socialized medicine, health insurance, or some form of government control? Are we to turn haphazardly to rapidly brought out schemes? Let the doctors speak, through their representative organizations, to retain for the practicing profession the control of the practice of medicine. A resolution for all of us for 1939—in the words of the Constitution of the American Medical Association—to "promote the science and art of medicine and the betterment of public health."

T. S. W.

HOSPITAL JOURNALS

MOST of us are familiar with certain institutional publications, such as those issued by the staffs of Johns Hopkins, the Mayo Clinic and a few other medical groups. However, for the most part, only the larger centers of medical teaching can afford this practice.

Therefore it was with interest that we received the first issue of the *Brooklyn Hospital Journal*, a quarterly of sixty to seventy pages of well presented information, dressed up nicely in a pigeon blue cover. Scientific articles are contributed by the men on the staff of the hospital, and one historical article appears in each number. The editor, Dr. Nathaniel P. Rathbun, well known to urologists throughout the country, has done a fine job with the seven papers of the introductory number. The printing is likewise excellent.

Congratulations to editor, contributors and staff! This is a move in the right direction, a practice that should be copied by other hospital groups throughout the land.

T. S. W.

ESSAY AWARD

THE Mississippi Valley Medical Society offers a cash prize of $100.00, a gold medal and a certificate for the best unpublished essay on a subject of interest and practical value to the general practitioner. Entrants must be members of the American Medical Association. Contributions must be not over 5,000 words in length, must be typewritten in English, and must be submitted in quintuplicate not later than May 1, 1939. The winner will be invited to present his paper before the next annual meeting of the Mississippi Valley Medical Society at Burlington, Iowa, September 27–29, 1939. The Society reserves the exclusive right to publish the essay first in its official publication.

Further information may be secured from Harold Swanberg, M.D., Secretary, Mississippi Valley Medical Society, 209 W.C.U. Building, Quincy Illinois.

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ORIGINAL ARTICLES

THE ASSOCIATION OF POLYCYSTIC DISEASE OF THE KIDNEYS WITH CONGENITAL ANEURYSMS OF THE CEREBRAL ARTERIES*

C. R. O'Crowley, M.D. and Harrison S. Martland, M.D.

NEWARK, NEW JERSEY

POLYCYSTIC disease of the kidney has occupied a prominent and interesting place in both the urologic and general medical literature of the past quarter of a century. During this period there have been great differences of opinion as to the etiology of the cystic kidney. It is generally believed that the cysts are retention cysts and depend upon obstruction at some point along the course of the uriniferous tubule.

The original theory of Virchow that kidney cysts were the outcome of an embryonal or fetal nephritis which caused a fibrosing papillitis, has been abandoned in favor of a theory based purely on developmental defects. The exact site and nature of the developmental fault, however, is still a matter of dispute.

Most workers agree that kidney cysts arise from a failure of proper fusion of the secretory and excretory systems (collecting tubules) during the embryonic formation of the kidney. This is a lack of union between the derivatives of the mesodermal nephrogenic cord and the ureteric buds. Oertel[1] states that incomplete convoluted tubules and loops, actual misdirection in the differentiation of the nephrogenic cell masses, abnormal mesodermal derivatives (muscular and mucoid tissue), abortive abbreviated ureteric buds, adenomatous growths, etc.—all have been found in polycystic kidneys. He further also states "The question whether there exist fundamental genetic differences in the formation of solitary cysts and the genuine polycystic kidney has been denied by the majority of investigators, who recognize only quantitative differences in these respects. On the other hand, some still emphasize the possibility of certain distinctions in the origin of these two types." Kampmeier[2] claims that this condition is caused by cystic atrophy of the first generation of excretory tubules, that these, instead of being lost, persist and thus prevent the formation of new functional collecting tubules.

However, despite these and many other controversial opinions, pathologists and urologists are today agreed that the polycystic kidney is congenital, developmental in origin and always bilateral.

The purpose of this paper is to add evidence for the theory of the congenital etiology of the polycystic kidney, by presenting the association of this condition with other congenital defects. Of greatest importance is the simultaneous occurrence of spontaneous subarachnoid hemorrhage caused by rupture of congenital "berry" aneurysms of the vessels of the base of the brain.

One of us (H. S. M.), as Chief Medical Examiner of Essex County (Newark) New Jersey, has observed fifty-four cases of spontaneous subarachnoid hemorrhage in a

* From the Departments of Urology and Pathology of the Newark City Hospital, and the Office of the Chief Medical Examiner of Essex County, Newark N. J. Read before the American Association of Genito-Urinary Surgeons, at Fiftieth Annual Meeting, Absecon, New Jersey, May 2, 1938.

series of more than 10,000 routine medico-legal autopsies performed during the past twelve years. In thirty-eight of these fifty-four cases a ruptured, congenital, berry aneurysm of the circle of Willis, at or near the bifurcation of its larger branches was found.

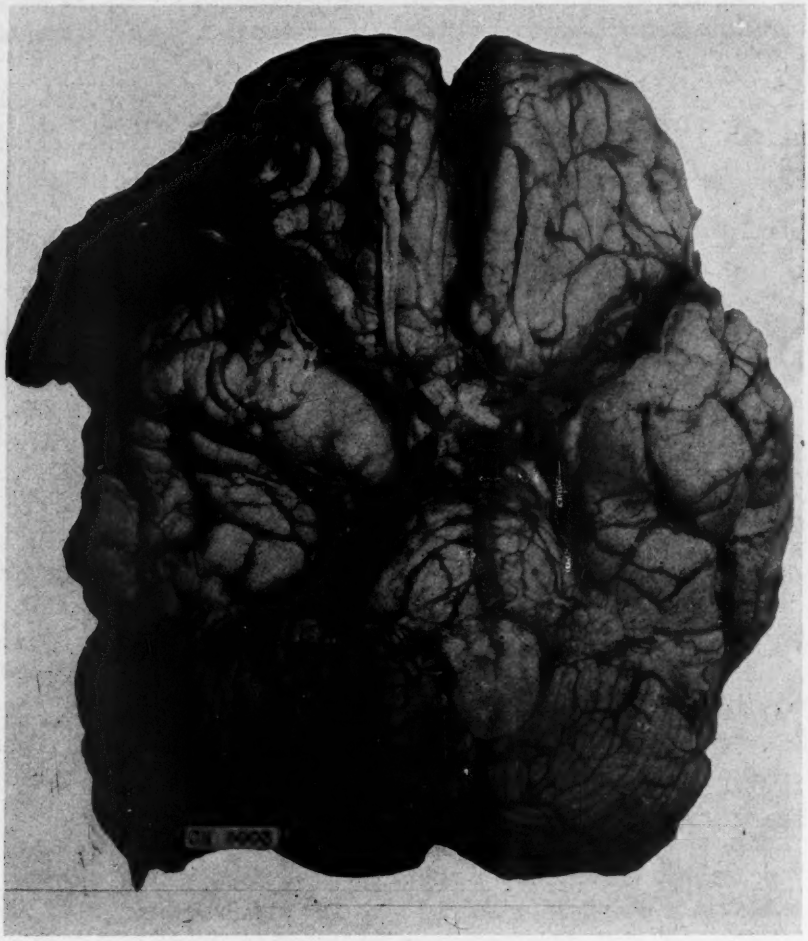

FIG. 1. Case 1. Brain showing spontaneous subarachnoid hemorrhage due to ruptured congenital aneurysm on right middle cerebral artery. Two unruptured aneurysms may be noted on left middle cerebral artery.

In seven of these instances in which a congenital aneurysm of the cerebral vessels was demonstrated, there were other associated congenital defects. Three showed large, bilateral, polycystic kidneys (two of these cases also had aberrant bile duct cysts of the liver) whereas four further cases revealed minor congenital defects—hypoplasia of left kidney; stenosis of abdominal aorta with hypoplasia of left kidney; and the presence of a Chiari's network in the right auricle; and finally a case showing abnormal position of both adrenals.

This illustrates the well recognized fact that congenital lesions, often of widely varying character, may frequently be found to occur simultaneously. Many instances in the literature illustrate the occurrence of two, and often multiple, defects in the same individual.

However, although we have found no specific reports in the literature per se of the simultaneous occurrence of polycystic kidneys and congenital cerebral aneurysms, a careful study of the literature reveals two such instances reported along with other congenital defects. The first such case was reported by Dunger[3] in 1904. This worker reports a father, son nad nephew who had

polycystic kidneys; the son died of an aneurysm of the middle cerebral artery. In 1905 Sieber[4] reported 212 cases of polycystic kidneys. Ten died of cerebral hemorrhage, yet no berry aneurysms were observed; the deaths were regarded as ordinary apoplexies resulting from the hypertension so frequently associated with late polycystic disease of the kidneys.

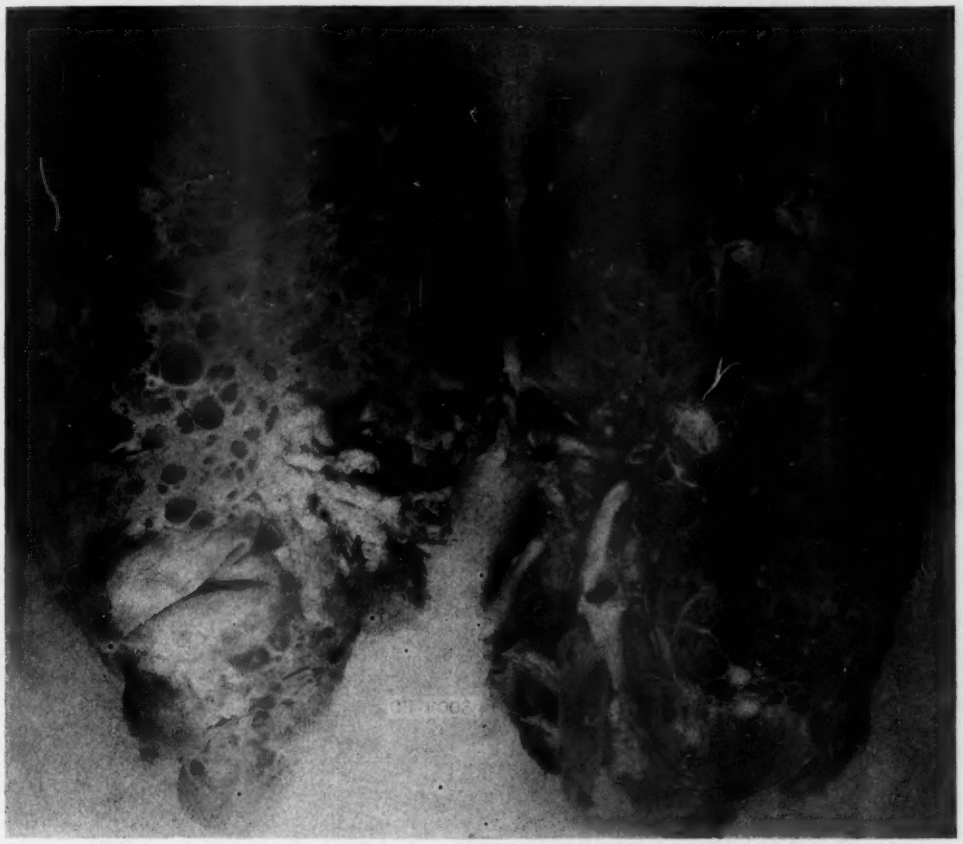

Fig. 2. Case 1. Congenital bilateral polycystic disease of kidneys. The left kidney weighed 480 Gm., the right kidney 490 Gm.

In 1909, Coombs[5] reported five deaths from cerebral hemorrhage in forty-two cases of polycystic disease of the kidneys. From autopsy reports, however, none of these could be identified with certainty as due to ruptured cerebral aneurysms of congenital origin; six appeared to have been caused by arteriosclerotic changes.

Fearnsides[6] in 1916 reported thirty-one cases of congenital cerebral aneurysms. In but seven of these were complete autopsies performed. In one case, the patient died of renal insufficiency due to congenital, bilateral polycystic disease of the kidneys. Autopsy revealed two small unruptured berry aneurysms, one at the junction of the left anterior cerebral and anterior communicating arteries, the other on the right middle cerebral artery. These were but incidental autopsy findings.

Katz and Müehe in 1924[7] reported a case of a woman who suffered from severe headaches since childhood and who died suddenly at the age of 45. At autopsy a ruptured aneurysm of the anterior communicating artery, and a second unruptured aneurysm at the junction of the internal carotid and right middle cerebral arteries were found, in association with congenital bilateral polycystic kidneys.

It may be said in summary, therefore, that of ninety cases of congenital cerebral aneurysms reported (in thirty papers) in the literature in which adequate autopsy protocols are available, there were only two

cases found of bilateral congenital polycystic disease of the kidneys associated with spontaneous subarachnoid hemorrhage.

FIG. 3. Case 1. Liver, showing extensive congenital aberrant bile duct cysts.

There are a large variety of other congenital defects which have been reported in association with congenital polycystic disease of the kidneys. Although most of these are of minor importance, gross defects, especially in the stillborn, showing extensive cystic disease of the kidneys and liver, are encountered. These defects occasionally interfere with the mechanism of labor.

Clinicians recognize that bilateral polycystic disease of the kidneys may exist throughout most of early adult life as an unsuspected condition. In most instances these individuals gradually develop renal insufficiency, which sooner or later leads to renal hypertension and secondary atheromatous changes in the cerebral and coronary arteries. Except for occasional renal hemorrhage or symptoms produced by pressure, the first evidence of the presence of this disease is often manifested by renal insufficiency, uremia, coma and death. Thus, such individuals often live to the fourth and fifth decades before symptoms of the disease present themselves. In some cases, however, because of the hypertension and associated blood vessel changes, death may result from cerebral hemorrhage or from coronary disease and its sequelae, rather than from uremia.

Many such cerebral deaths would be diagnosed clinically as ordinary apoplexy. Unless confirmed by autopsy, the accuracy of this diagnosis can never be proved, since some may be due to rupture of congenital aneurysms. Thus, when a cerebral hemorrhage occurs in an individual known to have congenital polycystic kidneys the possibility of subarachnoid hemorrhage due to associated defects in the cerebral arteries of congenital origin must be seriously considered.

THE ASSOCIATION OF POLYCYSTIC DISEASE OF THE KIDNEYS WITH CONGENITAL ANEURYSMS OF THE CEREBRAL ARTERIES

A review of the literature has revealed but two instances of death from subarachnoid hemorrhage caused by congenital cerebral aneurysms in which the autopsy also disclosed bilateral polycystic disease of the kidneys (Cases of Dunger, Katz and Müehe, quoted above).

Of the present series of fifty-four cases of spontaneous subarachnoid hemorrhage, in thirty-eight the bleeding was definitely caused by rupture of congenital berry aneurysms of the circle of Willis or its larger branches. Of these thirty-eight cases, congenital, bilateral polycystic disease of the kidneys was found at autopsy in three instances. Since it is not unusual to observe two or more congenital defects in the same individual, the association of polycystic kidneys and berry aneurysms in the same individual is evidence for the congenital origin of both conditions.

REPORT OF CASES

Case I. Ruptured congenital berry aneurysm of right middle cerebral artery with spontaneous subarachnoid hemorrhage. Bilateral, congenital polycystic disease of kidneys. Extensive aberrant bile duct cysts of liver. Congenital cyst of spleen. Unruptured berry aneurysm of left middle cerebral artery. No arteriosclerosis or syphilis.

The patient, a white male, 42 years of age, complained of frequent headaches and vertigo. He was suddenly seized with severe headache followed by unconsciousness and convulsions. On admission to the hospital he was in deep coma. The spinal fluid, which at this time contained blood, later became xanthochromic. He remained in deep coma until four days later when death occurred. Clinical diagnosis, spontaneous subarachnoid hemorrhage.

Necropsy. Brain. There was extensive subarachnoid hemorrhage over the inferior and lateral surfaces of the right frontal lobe with secondary rupture into the subdural space and brain parenchyma and an intracerebral clot 5 cm. in diameter. The right lateral ventricle was compressed and convolutions over the superior surface of the brain were flattened. A ruptured, lobulated, berry aneurysm of the right middle cerebral artery was found 2.5 cm. from the origin of this vessel. The aneurysm was 1 cm. in diameter, within the Sylvian fissure, and had ruptured on its superior surface. Two unruptured berry aneurysms, each 4 mm. in diameter, were observed on the left middle cerebral artery.

Kidneys. The left measured $14 \times 9 \times 5$ cm. and weighed 480 Gm. Most of the kidney parenchyma had been replaced by numerous cysts, ranging in size from those just visible to larger ones 1 cm. in diameter. Most of the cysts contained clear serous fluid, others opalescent, cloudy fluid. The right kidney measured $15 \times 7 \times 6$ cm., weighed 490 Gm., and showed the same general appearance and detail as the left kidney.

The liver was markedly enlarged and weighed 3,100 Gm. Both lobes contained innumerable cysts, varying in size from 1 mm. to 4 cm. These cysts contained watery or light yellowish fluid and were lined by smooth, glistening membrane.

The spleen was normal in size and contained a solitary cyst 1.5 cm. in diameter. No hypertrophy of the left ventricle was present and there was no evidence of syphilis or arteriosclerosis except for an occasional yellow streak of atheroma in the aorta.

Case II. Ruptured congenital berry aneurysm of anterior communicating artery with spontaneous subarachnoid hemorrhage. Bilateral, congenital, polycystic disease of kidneys. Aberrant bile duct cyst of liver. Surgical decompression. Obesity. No arteriosclerosis or syphilis.

A female, white, 56 years of age, was found on the floor of her bathroom where she had apparently fallen, receiving a laceration of the scalp. She was admitted to the hospital in coma, with stiff neck, fever and high blood pressure. The spinal fluid was bloody. A diagnosis of possible traumatic cerebral hemorrhage was made and left temporal decompression performed. The woman lived three days.

Necropsy. Brain. Extensive subarachnoid hemorrhage was present over the inferior surface of both frontal lobes, extending over the base of the brain and lateral surfaces. A ruptured berry aneurysm, 8 mm. in diameter, on the anterior communicating artery near the

left anterior cerebral was accompanied by secondary intracerebral hemorrhage in the left frontal lobe, breaking into the anterior horn of the left lateral ventricle, with extensive interventricular hemorrhage.

Kidneys. The left kidney measured 17 × 10 × 8 cm. and weighed 600 Gm. It was the seat of innumerable small and large cysts, containing clear serous fluid and yellowish and brownish fluid forming a display of color in the cut section of the kidney. Very little kidney parenchyma was recognizable. The right kidney measured 15 × 9 × 6 cm., weighed 510 Gm., and had the same general appearance as the left.

The liver showed one aberrant bile duct cyst 3 cm. in diameter.

The rest of the autopsy was essentially negative except for obesity and evidence of recent surgical decompression. There was no hypertrophy of the left ventricle, no evidence of syphilis or arteriosclerosis.

Case III. Ruptured congenital berry aneurysm of right middle cerebral artery with spontaneous subarachnoid hemorrhage and secondary hemorrhage in lateral ventricle and subdural space. Congenital polycystic disease of kidneys. No arteriosclerosis or syphilis.

Male, white, 27 years of age had sudden onset of severe headache followed by restlessness, tenderness and rigidity in neck, and unconsciousness. He was admitted to the hospital where he remained in deep coma and died two and one-half days later.

Necropsy. Brain. There was extensive subarachnoid hemorrhage over the inferior surface of the right frontal and temperosphenoidal lobes, extending over the base and lateral surfaces of the brain. A ruptured berry aneurysm 3 mm. in diameter was found on the right middle cerebral artery near the junction of the internal carotid. Secondary hemorrhage into the cerebrum had occurred, breaking into the right lateral ventricle and into the right subdural space.

Kidneys. The left kidney measured 19 × 9 × 7 cm. and weighed 650 Gm. The whole kidney was the seat of extensive small and large cysts, and very little recognizable kidney parenchyma remained. The right kidney measured 21 × 10 × 8 cm. and weighed 800 Gm., and had the same appearance as the left.

No hypertrophy of the left ventricle and no evidence of syphilis or arteriosclerosis were present except for an occasional patch of soft atheroma in the aorta and coronary arteries.

OTHER CONGENITAL DEFECTS ASSOCIATED WITH CONGENITAL ANEURYSMS OF THE CEREBRAL ARTERIES

Congenital Hypoplasia of Kidney. In this series of fifty-four cases of spontaneous subarachnoid hemorrhage in which a congenital aneurysm was the source of the bleeding in thirty-eight instances, a congenital hypoplasia of the kidney was observed twice.

Case I. Ruptured congenital berry aneurysm of right middle cerebral artery with spontaneous subarachnoid hemorrhage and secondary hemorrhage into brain parenchyma and subdural space. Congenital hypoplasia of left kidney. Congenital stenosis of abdominal aorta. Compensatory hypertrophy of right kidney.

A white male, 20 years of age, fell while at work in a chemical dye plant. Convulsions and unconsciousness resulted and he died five minutes after admission to the hospital.

Necropsy. Extensive spontaneous subarachnoid hemorrhage was seen over the base of the brain with secondary hemorrhage in the right temperosphenoidal lobe and the subdural space. A ruptured berry aneurysm, 1 cm. in diameter, was present on the right middle cerebral artery, and an unruptured aneurysm, 0.5 cm. in diameter, on the left vertebral artery.

Congenital hypoplasia of the left kidney, which was a miniature kidney with fetal lobulations well retained, patent ureter and congenital stenosis of the abdominal aorta, admitting only the tip of finger, opposite the left renal artery were other congenital anomalies. Compensatory hypertrophy of the right kidney had occurred.

Case II. Ruptured congenital berry aneurysm of left vertebral artery with spontaneous subarachnoid hemorrhage. Congenital hypoplasia of left kidney with compensatory hypertrophy of right kidney.

A male, white, 40 years of age, was found dead in his automobile.

Necropsy. Extensive spontaneous subarachnoid hemorrhage was found over the base of the brain, most marked about the pons and medulla. There was a ruptured berry aneurysm

of the left vertebral artery 4 mm. in diameter, associated with congenital hypoplasia of the left kidney, miniature kidney, with small renal artery, ureter patent. There was compensatory hypertrophy of the right kidney. Chronic pulmonary tuberculosis was a further finding.

Other Congenital Defects. From reports in the literature, the most frequent congenital lesion found in association with congenital cerebral aneurysms has been coarctation of the aorta. Maude Abbott in 1928,[8] in a series of 200 collected cases of coarctation of the aorta, reported eighteen cases in which death was due to rupture of a congenital cerebral aneurysm. Baker and Sheldon in 1936[9] reported similar cases from the literature.

As noted above, in one case in the present series, the adrenal glands were not in their normal position. The main portion of both glands was situated beneath the capsule of the kidneys. We have observed this anomaly with sufficient frequency during routine autopsies to add support to the original theory of Grawitz, who in 1883, claimed that the so-called hypernephromata, especially those occurring in the upper pole of the kidney, might well be derived from ectopic rests or remnants of adrenal cortex. For this reason we do not favor entire abandonment of the Grawitzian theory for the more dogmatic one which holds that all hypernephromas are renal carcinomas. In spite of perennial argument on this subject in many publications, renal tumors often defy diagnosis and strict pathologic classification.

REFERENCES

1. Oertel, Horst. Special Pathological Anatomy. Montreal, 1938, Renouf Publishing Co., pages 324–325.
2. McKenna, C. M., and Kampmeier, O. F. A consideration of the development of polycystic kidney. *J. Urol.*, 32: 37, 1934.
3. Dunger, K. Lehre von den Cystenniere. *Beitr. z. path. Anat. u. z. alg. Path.*, 35: 445, 1904.
4. Sieber, F. Über Cystennieren bei Erwachsenen. *Deutsche Ztschr. f. Chir.*, 79: 406, 1905.
5. Coombs, Carey. Polycystic disease of the kidneys. *Quart. J. Med.*, 3: 30, 1909–1910.
6. Fearnsides, E. G. Intracranial aneurysms. *Brain*, 39: 224, 1916.
7. Katz, Georg, and Müehe, Erich. Kongenitale Cystennieren mit Hypertonie und Folgezustanden. *Ztschr. f. Urol.*, 18: 453, 1924.
8. Abbott, M. E. Coarctation of the aorta of the adult type. II. A statistical study and historical retrospect of 200 recorded cases, with autopsy, of stenosis or obliteration of the descending arch in subjects above the age of two years. *Am. Heart J.*, 3: 392, 574, 1928.
9. Baker, T. W., and Sheldon, W. D. Coarctation of the aorta with intermittent leakage of a congenital cerebral aneurysm: report of a case. *Am. J. M. Sc.*, 191: 626, 1936.

SPONTANEOUS SUBARACHNOID HEMORRHAGE AND CONGENITAL "BERRY" ANEURYSMS OF THE CIRCLE OF WILLIS*

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OF 10,000 routine autopsies performed by the Office of the Chief Medical Examiner of Essex County, New Jersey from 1925 to 1938, 7,500 involved homicide, suicide, highway accident, or other form of violent death. The balance, 2,500 investigations, were instances of sudden or unexplained death, in which autopsy revealed that death was due to natural causes. In this latter group, there were fifty-four cases of spontaneous subarachnoid hemorrhage. Thus in every 100 sudden or unexplained deaths, we should expect to encounter two cases of spontaneous subarachnoid hemorrhage.

A study of these fifty-four cases of spontaneous subarachnoid hemorrhage revealed the association of congenital aneurysms of the circle of Willis and polycystic disease of the kidney, as reported in the preceding paper. The more detailed study of these cases is here made the subject of a separate publication since spontaneous subarachnoid hemorrhage is of interest to diagnosticians, surgeons, and neurologists, whereas the previous study is of greatest value to urologists.

SPONTANEOUS SUBARACHNOID HEMORRHAGE

DEFINITION

In spontaneous subarachnoid hemorrhage (in which there is no disease of the brain, meninges or skull) the bleeding occurs between the arachnoid and the pia mater. This takes place almost always at the base of the brain, and though the blood spreads widely, it is still confined to the subarachnoid space. If the hemorrhage be of large amount, the blood may follow this potential space and spread over the lateral and superior surfaces of the brain, and even extend down the brain stem, producing rapid death by compression of the medullary centers. Finally, the extravasated blood may rupture into the subdural space or into the brain parenchyma, and may by this route burst into the lateral ventricles.

The application of the term "spontaneous" to this form of subarachnoid hemorrhage is not accurate, since most cases are due to the rupture of preëxisting aneurysms of the cerebral arteries. However, because of common usage, any attempt to abandon or alter the terminology would only lead to confusion.

Spontaneous subarachnoid hemorrhage must be differentiated from forms of traumatic subarachnoid and intracerebral hemorrhage. The former results from direct or contrecoup laceration of the cerebral cortex (usually associated with fracture of skull), whereas the latter are hemorrhages which originate within the brain substance as a result of ordinary apoplexy, telangiectatic brain tumors, or deep traumatic lesions of the parenchyma (any of these may secondarily break into the subarachnoid space—secondary subarachnoid hemorrhage).

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Read before the American Association of Genito-Urinary Surgeons, Absecon, New Jersey, May 2, 1938, as a portion of the preceding paper "The Association of Polycystic Disease of the Kidneys with Congenital Aneurysms of the Cerebral Arteries."

INCIDENCE

Spontaneous subarachnoid hemorrhage has long been regarded as a rare condition, and one which is chiefly of pathologic interest. However, since pathologists have called attention to this condition, and since lumbar puncture has become a common diagnostic procedure, the clinical diagnosis of this condition is a more frequent occurrence.

Fatal Cases. In spontaneous subarachnoid hemorrhage the onset is sudden and soon followed by death. Therefore, the medical examiner and coroner's physician see more instances of this condition than are to be observed in routine hospital or private practice. As noted above, in our experience, 2 per cent of sudden deaths are caused by rupture of aneurysms of the circle of Willis and its larger branches. The age, sex and race of fifty-four fatal cases are indicated in Table 1.

Table 1

AGE, SEX AND RACE IN FIFTY-FOUR DEATHS FROM SPONTANEOUS SUBARACHNOID HEMORRHAGE

	Cases
Age	
10 to 20 years	5
20 to 30 years	13
30 to 40 years	7
40 to 50 years	12
50 to 60 years	13
60 to 70 years	4
Sex	
Males	27
Females	27
Race	
White	45
Colored	9

The youngest fatality in this series was at the age of 14, the oldest 67 years, whereas the greatest incidence is in the third, fifth and sixth decades. In the second decade, congenital hypoplasia of the cerebral arteries, without aneurysm, but often associated with status lymphaticus, account for most of the deaths.

Spontaneous Subarachnoid Hemorrhage Followed by Recovery. Ayer,[1] along with many other clinicians, believes that 50 per cent of patients with spontaneous subarachnoid hemorrhage may recover. And, Bramwell,[2] states, that although the onset is abrupt and the patient unconscious, those individuals who recover, do so quickly—there is only a short period of unconsciousness. "He may be drowsy or stuporous; sometimes he is confused, irritable, and resistive; and he usually complains of 'terrible' headache. . . . The extravasation in such cases has not been excessive and the fact that the patient is now conscious or less drowsy suggests that the hemorrhage has been arrested." The symptoms in such cases have, for the most part been attributed to a small extravasation from a cerebral aneurysm.

However, in our opinion these cases are not due to leaking or ruptured congenital aneurysms. We believe some other less serious lesion must account for these smaller and more localized hemorrhages, from which patients may recover. This opinion is based upon the fact that the pathologic residua of healed ruptured aneurysms are rarely seen in large autopsy services (brown stains in leptomeninges due to hemosiderin deposits in the region of the aneurysm). There is little anatomic proof that "berry" aneurysms rupture and heal, and less proof that these aneurysms may become thrombosed and absorbed. It is interesting to note that Boyd[3] states, "These aneurysmal cases are usually fatal. There is another group of cases which usually recover and are probably due to some rather mild infection, some meningoencephalitis, which especially attacks the vessels. They occur in groups of little epidemics, a fact which serves to strengthen the idea that they are infectious, although of this there is no direct proof."

The recent recognition of obscure cases of (microscopic) necrotizing arteritis* may possibly account for some of these cases.

PATHOLOGY

The pathologic lesions in fifty-four fatal cases of spontaneous subarachnoid hemorrhage are detailed in Table 11.

* An infectious, often widespread disease of the smaller arteries which some believe to be a form of periarteritis nodosa caused by rheumatic virus, allergy or what-not.

TABLE II
ANALYSIS OF PATHOLOGIC LESIONS FOUND IN FIFTY-FOUR CASES OF FATAL SPONTANEOUS SUBARACHNOID HEMORRHAGE

Ruptured congenital "berry" aneurysms	38
Undetermined source of bleeding (Small aneurysms probably not discovered at autopsy)	5
Ruptured hypoplastic cerebral arteries (Associated usually with status lymphaticus)	9
Ruptured aneurysm due to arteriosclerosis	1
Ruptured arteriosclerotic vessel	1
	54

Extensive spontaneous subarachnoid hemorrhage is usually due to rupture of a congenital aneurysm of one of the larger cerebral arteries in or near the circle of Willis. When the aneurysm is not found at autopsy, either it may have been missed due to lack of proper autopsy technique, or else the defect may be overlooked because the aneurysm has entirely "blown out" and is lost in the torn tissues and surrounding hemorrhage.*

Spontaneous subarachnoid hemorrhage in association with congenital hypoplasia of the cerebral arteries and often with status lymphaticus (a condition which the author still believes exists), often show parenchymal hemorrhage, most frequently in the cerebellum and occipital lobes. It is questionable whether all of these cases should be included in this series, since the subarachnoid hemorrhage is occasionally secondary. One of these patients also showed congenital cystic disease of the lungs, and still another, a moderate degree of subaortic stenosis (another congenital lesion).

Since almost all cases of fatal spontaneous subarachnoid hemorrhage are caused by a rupture of an aneurysm of the cerebral arteries and in the majority of cases such an aneurysm when it occurs in or near the circle of Willis is due to a congenital defect in the arterial wall, a discussion of the pathogenesis of cerebral aneurysm is in order.

Congenital or "Berry" Aneurysms. In 1887, Eppinger[4] first suggested that the small saccular aneurysms of the circle of Willis or its larger branches (particularly at the bifurcations) were congenital defects of the arterial wall. Eppinger called these "berry" aneurysms because of their shape and color. Such aneurysms are usually small, from 3 mm. to 1 cm. in diameter, and have the appearance of a small berry. They are most commonly found on the main vessels of the circle of Willis or on its larger branches, usually, but not always at or near the bifurcation of a large vessel. These defects may be sometimes multiple, and occasionally are encountered as incidental autopsy findings during routine autopsies.

In 1930, Forbus[5] demonstrated that the arterial walls in this condition characteristically lack a muscular coat at the point of sacculation of these aneurysms. He pointed out that such a defect might arise from failure of proper embryonic fusion of the separately developed muscle coats of the main vessels and its branches. From microscopic studies Forbus further concluded that these aneurysms developed from a combination of two factors: a focus of weakness in the vessel wall as a result of the defect in the muscularis, and subsequent degeneration of the intimal elastica because of continued stretching due to the blood pressure.

Recently Helpern[6] has again emphasized the importance of the recognition of these congenital berry aneurysms as a cause of sudden death and supports the views of Forbus as to their pathogenesis. Helpern, on microscopic examination of these aneurysms, found that the aneurysmal wall was almost devoid of both the internal elastica and the muscularis, and was composed of a slightly thickened continuation of the intima and adventitia. Furthermore, he calls attention to the fact that occasionally when these lesions are near the surface of

* It has been our practice when diffuse subarachnoid hemorrhage is found at autopsy over the base of the brain to turn the base upward and gently spread it apart by placing a block of wood beneath it. Blunt dissection and scraping of the entire circle of Willis and its larger branches, using a scalpel and a fine stream of water will usually reveal the aneurysm. This is important, since innocent persons have been convicted of manslaughter in assault cases due to the bungling methods of some pathologists.

the brain, rupture may produce a large subdural hemorrhage with little or no subarachnoid bleeding, and in such cases the spinal fluid may contain no blood whatsoever.

Other workers claim, however, that these microscopic findings are often difficult or impossible to demonstrate and that such medial defects may often be very irregularly distributed. Karmally and Manohar,[7] though believing that most of these aneurysms are congenital, still claim that the defects of the media do not fully explain their formation. These observers hold that the embryologic theory of the cause of these defects will not always explain the formation of berry aneurysms, since the imperfections in the media may occur some distance from the site of branching of the vessels, which is the common location of berry aneurysms. They conclude that further histologic studies are necessary before congenital aneurysms can be satisfactorily explained.

Most pathologists, however, believe that these lesions are of congenital origin, and that rupture of such berry aneurysms is the most common cause of fatal spontaneous subarachnoid hemorrhage in either the young or old who are free of syphilis or arteriosclerosis.

Of the fifty-four cases dying of spontaneous subarachnoid hemorrhage reported herein, these congenital berry aneurysms were found in thirty-eight; in eleven cases the hemorrhage was due to other lesions, and in the remaining five, no aneurysm or other lesions could be discovered or identified. (See Table II.)

Aneurysms Due to Arteriosclerosis. Extensive atheroma of the arteries at the base of the brain may cause aneurysmal dilatation of the vessel or an actual aneurysm. These lesions are often larger than a berry aneurysm and occasionally may cause symptoms of intracranial pressure before rupture occurs. These may occasionally be diagnosed from the history, or from the presence of paralysis of the third and sixth cranial nerves.

In this series of fifty-four cases of spontaneous subarachnoid hemorrhage there was but one aneurysm due to arteriosclerosis. This occurred in a white female, age 54, who died suddenly. Autopsy revealed hypertensive cardiovascular disease and a large, irregular aneurysm of the basilar artery, 2 cm. in diameter, surrounded by extensive subarachnoid hemorrhage.

Aneurysms Due to Syphilis. Syphilis is but rarely the cause of aneurysms at the base of the brain. Fearnsides in 1916[8] found that in his cases that syphilis could seldom be identified as a possible etiologic factor in the production of these aneurysms. He felt that when these occurred, the lesions were chiefly of the basilar or vertebral arteries, and grew to such size as to give rise to pressure symptoms before rupture.

Martland in 1932[9] has stated that "Syphilis is frequently seen in the cerebral arteries as a periarteritis, and because of the small caliber of the vessels, an added obliterating endarteritis is liable to produce thrombosis rather than aneurysm (Endarteritis obliterans luetica of Heubner)."

In this series of cases of spontaneous subarachnoid hemorrhage, there were none which could be attributed to syphilis.

Mycotic Aneurysms. In rare instances an infected embolus (usually as a complication of subacute bacterial endocarditis) may cause subarachnoid or intracerebral hemorrhage either by the production of a mycotic aneurysm or as the result of so-called toxic effects on the walls of the capillaries, without the actual formation of an aneurysm. When the hemorrhage is extensive, the presence of such aneurysms is very difficult to ascertain.

Of the fifty-four cases suffering from spontaneous subarachnoid hemorrhage here discussed, none were due to mycotic aneurysms, although sudden death from intracerebral hemorrhage in subacute bacterial endocarditis has been observed a number of times during the past twelve years.

Other Causes. Spontaneous subarachnoid hemorrhage may occasionally occur

in leucemia, purpura and sometimes in septicemia, without any demonstrable gross lesion in the brain or meninges. These are usually attributed to the hemorrhagic diathesis, but occasionally in leucemia microscopic sections may show thrombosis of capillaries by leucemia cells. The possibility of infectious necrotizing arteritis causing subarachnoid hemorrhage has been noted above.

Relation of Trauma. In our series, twenty-one of the fifty-four patients with spontaneous subarachnoid hemorrhage gave some history of falls or minor injuries —in street, bathroom, after fist fight, bumping head in train, while fighting fire, etc. However, careful autopsies failed to reveal any serious injuries. In most cases the onset is sudden, and with the rupture of the aneurysm the patient often falls and sustains an injury. Since almost every known disease has been attributed to trauma in the compensation courts, and substantial awards have often been given, it is easily seen how involved this problem may become.

In most arguments before compensation courts regarding the relation of trauma to disease, two important questions always arise. Was the injury the direct cause of the disease, and if not, did it aggravate the preëxisting condition. There are some workers who still believe that berry aneurysms may occasionally result from or follow a head injury. However, we do not feel that this view is tenable in the light of careful pathologic studies of this problem. We have never encountered an aneurysm of the circle of Willis which could be proved to originate as the direct result of an injury.

Berry aneurysms usually rupture spontaneously. There is no doubt, however, that in some cases actual rupture may be precipitated by trauma, or physical exertion, and especially trivial exertions which produce a rise in blood pressure, such as straining at stool, lacing shoes, sexual intercourse, sneezing, etc. Trauma can rarely be considered a causal agent and while the above conditions may have some medicolegal importance the same catastrophe occurs during sleep. The rupture is usually so abrupt, often with no apparent determining factor, that the attack is of the nature of an accident.

In summary it may be stated that aneurysms tend to rupture because of: superimposed changes in the vessel wall; increased blood pressure; in a few cases because of physical effort, strain, emotions, or rarely, because of trauma.

SYMPTOMS AND PHYSICAL SIGNS

As recently as 1934, Garvey[10] reviewed the clinical symptoms, etiology and pathologic findings in aneurysms of the circle of Willis and stated that "the diagnosis of intracranial aneurysm cannot be made with any degree of certainty until rupture occurs." The clinical syndrome produced by rupture, however, is usually characteristic.

The symptoms of rupture are often dramatic. Howell[11] states, "The patient calls out in pain, and may then fall unconscious; indeed, the diagnosis is often made on the history of a cry of 'Oh! my head!' followed by unconsciousness." Bramwell[2] states that the patient may be in robust health or may have complained of premonitory headache for some time, when he is suddenly seized with an intense "throbbing" or "bursting" headache, often accompanied by vertigo and vomiting. This is followed almost immediately by coma. The breathing becomes stertorous, the pupils dilated, the pulse slow and perhaps irregular, and the temperature usually rises. Neck rigidity and Kernig's sign are often present; the patellar reflexes are diminished or absent, the plantar reflexes are frequently extensor in character, and ophthalmoscopic examination may reveal hemorrhages in the retina. If the patient becomes deeply comatose, the prognosis is extremely grave.

The characteristic syndrome of rupture of an aneurysm of the circle of Willis then consists of sudden headache, vomiting, followed quickly by an apoplectic seizure with rapid loss of consciousness, at times

convulsions, and deep coma. If death does not ensue, the patient may regain consciousness. This is apt to be followed by severe headache, photophobia, stiffness of the neck and other signs of meningeal irritation.

Examination of the spinal fluid during the first twenty-four to forty-eight hours after the rupture shows a uniformly bloody fluid under increased pressure. Later the spinal fluid may become xanthochromic. If there is doubt as to whether the blood in the spinal fluid is the result of the lumbar puncture, this question can be settled by comparing the depth of color of each of two or three samples collected in separate test-tubes. After standing, the supernatant spinal fluid will be yellow-tinged in cases of subarachnoid hemorrhage, but colorless after "traumatic" puncture.

Large hemorrhages are sometimes found in the retina, especially around the optic disk. The mechanism of the production of these hemorrhages is not clear, and they have been attributed to extravasation of blood along the optic nerve sheath or to obstruction of the central retinal vein within the optic sheath, with resulting venous stasis. Papilledema, as a rule, is absent.

In addition, certain localizing signs may be present, either before or after rupture, depending upon the site and size of the aneurysms. Aneurysms of the internal carotid artery within the cavernous sinus or just at the entrance into the cranial cavity are more apt to produce oculomotor paralysis with ptosis and iridoplegia. The paralysis occurs on the side of the aneurysm. These aneurysms may give rise to exophthalmos, amblyopia, and hemianopsia. Rupture into the cavernous sinus causes pulsating exophthalmos.

Aneurysms of the internal carotid artery at the point of origin of posterior communicating, ophthalmic, anterior and middle cerebral arteries, are more apt to produce ocular syndromes of the chiasmal or prechiasmal type with characteristic field defects rather than cranial nerve palsies.

Friedman[12] states:

"That aneurysms of the anterior cerebral artery may compress the optic and olfactory nerves. In the middle cerebral artery, it may involve the olfactory nerve in addition to the oculomotor. The pressure is, for the most part, exerted on the brain substance and gives rise to aphasia, monoplegia, or hemiplegia. Aneurysm of the posterior communicating artery may produce hemianopsia by implication of the optic tract.

"Aneurysm of the basilar artery exerts pressure chiefly against the pons, medulla, or peduncle. The patient with such a lesion usually experiences pain in the occipital region and difficulty in moving the head. Compression of the pons with symptoms of alternating subacute hemiplegia or bulbar paralysis may be evident. Manifestations of irritation or paralysis are sometimes referable to the individual cranial nerves. In aneurysm of the basilar artery the hemiplegia shifts from one side to the other without ever disappearing completely until finally the condition becomes a diplegia or paraplegia. Vomiting and respiratory embarrassment are particularly apt to occur in these cases.

"Aneurysm of the vertebral artery evokes similar symptoms, and in some individuals the palate and vocal cord on one side and the hypoglossus on the other side may be involved."

Most such localizing signs, however, are observed when larger aneurysms are situated on the internal carotid or at the origin of its larger branches and are of little diagnostic use in the vast majority of intracranial aneurysms which occur on the circle of Willis and which, as a rule, are symptom free until rupture occurs.

DIAGNOSIS

The diagnosis of aneurysm of the circle of Willis cannot usually be made before rupture. However, the diagnosis after rupture can often be made with a considerable degree of certainty. The characteristic clinical syndrome is described above, and

the differential diagnosis of coma, without a history of syphilis or hypertension, should include a consideration of this condition. If the coma is deep, this disease must be distinguished from cerebral hemorrhage (apoplexy). Symptoms pointing to the region of the internal carotid (oculomotor signs or trigeminal phenomena) are highly suggestive. If in addition we find retinal hemorrhages, bloody or xanthochromic spinal fluid, the diagnosis of subarachnoid hemorrhage may be made.

Spontaneous subarachnoid hemorrhage must also be differentiated from subdural hematomas and other forms of traumatic intracranial hemorrhage, from the various types of ophthalmoplegia, from migraine with or without ophthalmoplegia, from tumor of the trigeminal nerve and from infectious meningitis.

Lately it has become possible to diagnose a small number of unruptured intracranial aneurysms. This is made possible by careful neurologic examinations, expert roentgenographic and encephalographic studies, and arteriograms. However, these few instances are chiefly aneurysms situated on the internal carotid artery or at the origin of its main branches. These defects reach a large size and impede the surrounding circulation, press upon cranial nerves and erode adjacent bone. Unfortunately, these represent a very small number of intracranial aneurysms and are reported, for the most part as individual cases, by neurologists (often to demonstrate their skill in the localization of cerebral lesions).

In 1926, Sosman and Vogt[13] described the roentgenographic diagnosis of unruptured aneurysms of the circle of Willis. They state:

"The recognition of these aneurysms on Roentgen examination is by means of (1) calcification in the wall of the aneurysm, or (2) erosion of the bone adjacent to the aneurysmal sac. In the first, one can see thin plaques of calcium, usually semilunar in shape, with their convexity upward, lying beside the sella, or should the aneurysm be large, rising above the level of the sella, but just to one side of it. These are fine curvilinear shadows, sharply outlined, occasionally segmented, and easily recognizable as being in the wall of a cystic or rounded structure. . . . The erosion due to these pulsating sacs. . . . involves or may involve one anterior clinoid, the lateral half of the body of the sphenoid on the same side, and a similar portion of the posterior clinoid. . . . There is no expansion of the pituitary fossa . . . and no apparent depression of the floor of the fossa. The opposite anterior clinoid is not involved . . . and there is no pressure atrophy or forward bending of the posterior clinoid."

Such calcific deposits in the wall of the aneurysm, revealed by roentgenograms as concentric circular shadows, are known as Albl's rings. Further, the injection of thorotrast into the internal carotid artery followed by roentgenography may outline some aneurysms.

PROGNOSIS

It is of interest to note the duration of life in the fifty-four cases of spontaneous subarachnoid hemorrhage herein reported. They are tabulated in Table III.

Table III
DURATION OF LIFE IN FIFTY-FOUR CASES OF SPONTANEOUS SUBARACHNOID HEMORRHAGE

	Cases
Sudden death	21
(Found dead, dying within thirty minutes after collapse, dead on arrival at hospitals, etc.)	
Slower death	33
Lived approximately	
1 hour after attack	6
2 hours after attack	6
3 hours after attack	5
3–12 hours after attack	3
1 day after attack	4
2 days after attack	2
3 days after attack	2
4 days after attack	2
5 days after attack	1
6 days after attack	2

The patients lived six days, this being the longest duration of life in this series.

Most authorities agree that though many patients with spontaneous subarachnoid

hemorrhage die suddenly, the majority may live a sufficient length of time to remove them from the classification of "sudden deaths." In many cases classified as sudden death, such as those found dead in bed or at home, etc., it is often difficult to ascertain just how long the patient has survived after the rupture of the aneurysm. There is strong evidence, however, that many die shortly after the onset, and such individuals fall in the street or at home, are picked up dead, or are dead on arrival at hospitals. They almost never die instantaneously, however, and many survive minutes, hours or longer. In our experience, one-half of the fatal cases of spontaneous subarachnoid hemorrhage died within an hour of the rupture, the rest lived a few hours or days, but rarely longer than one week.

We are extremely doubtful about the presence of intracranial aneurysms in that 50 per cent of cases of spontaneous subarachnoid hemorrhage which are reported to have recovered.

CONCLUSIONS

1. Many of the observations in this series are at variance with descriptions of intracranial aneurysms given in textbooks and in the literature.

2. Practically all cases of fatal subarachnoid hemorrhage are caused by rupture of intracranial aneurysms.

3. We believe that most of those cases of spontaneous subarachnoid hemorrhage which recover (50 per cent according to some clinicians) are probably not due to "leaking" or ruptured intracranial aneurysms, but rather to some unexplained infection or to some as yet unknown cause. There is little anatomic proof that intracranial aneurysms leak, rupture and heal, or bleed at various intervals, and less proof that intracranial aneurysms may become thrombosed and disappear.

4. In our experience, by far the most common type of intracranial aneurysm is the congenital "berry" aneurysm of the circle of Willis and its larger branches. Such aneurysms are usually saccular, often multiple, and microscopic examination shows little or no evidence of inflammation. Usually the aneurysmal wall is almost devoid of muscularis and internal elastica. These aneurysms are not always situated at the bifurcation of large branches of the circle of Willis.

Contrary to the view of most authorities, there is no predilection for any particular branch of the circle of Willis nor for either side of the brain. A large series shows that these sacculations occur more or less symmetrically over the whole circle of Willis. (See Fig. 1.) They are infrequent on the internal carotid artery.

In addition, the association of this condition with other congenital defects, such as polycystic disease of the kidney and liver, as well as other renal anomalies, further supports the theory of congenital origin.

Intracranial aneurysms due to arteriosclerosis (cerebral atheroma), syphilis, bacterial endocarditis, and other causes are so rare that these types are of little practical importance as a cause of fatal subarachnoid hemorrhage. When such aneurysms do occur, however, they are usually situated on the deep cerebral arteries and when rupture occurs, they cause primary hemorrhage within the brain substance, often accompanied by secondary hemorrhage into the subarachnoid space.

5. Aneurysms of the circle of Willis rarely give rise to symptoms before rupture, and the majority will defy recognition. Those few diagnosed before rupture are larger aneurysms, situated often on the internal carotid arteries or near their main branches, which by pressure on circulation or on nerves, or by erosion of bone, give rise to localizing symptoms and signs. These are chiefly of neurologic interest.

6. When an aneurysm of the circle of Willis ruptures, a characteristic syndrome results which makes the diagnosis of this condition more or less certain.

7. We believe that trauma is never the direct cause of aneurysms of the circle of Willis. However, undue exertion, emotions,

trauma, or anything that may raise the blood pressure, may precipitate rupture and thus assume some medicolegal importance.

9. In this series of fifty-four cases of spontaneous subarachnoid hemorrhage there is no special sex or race distribution.

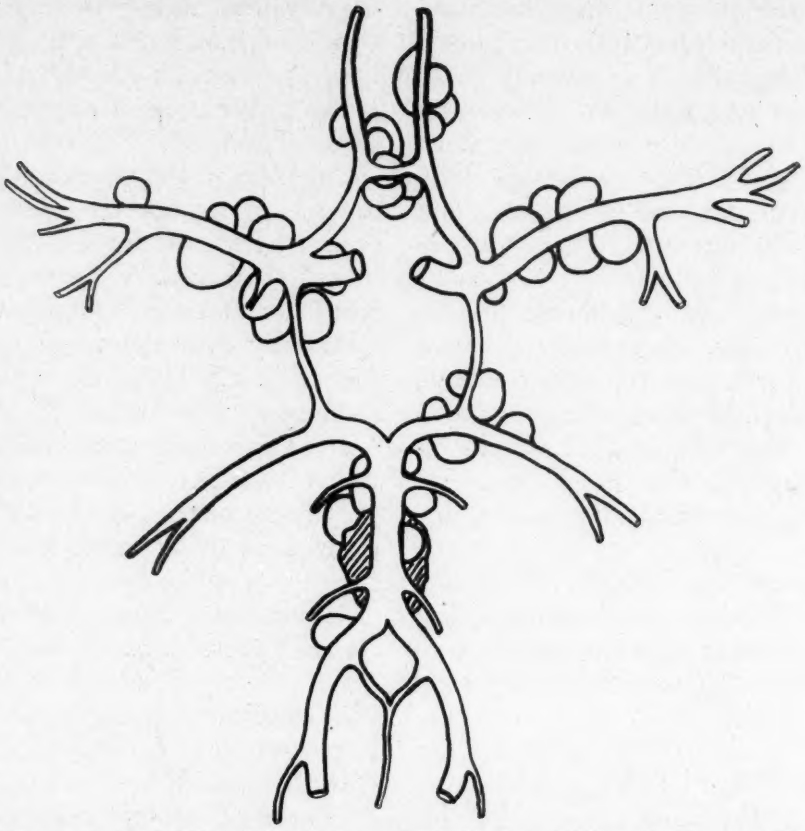

FIG. 1. Circle of Willis with position and relative size of thirty-eight congenital "berry" aneurysms, found at autopsy in fifty-four cases of spontaneous subarachnoid hemorrhage. A larger aneurysm (shaded) on the basilar artery, due to arteriosclerosis, is also shown.

Contrary to most authorities, it may be noted that there is no predilection for any particular branch of the circle of Willis nor for either side of the brain. A large series shows that these congenital berry aneurysms occur more or less symmetrically over the whole circle of Willis and its branches. They are infrequent on the internal carotid arteries.

The same arguments can be advanced for many coronary attacks. However, the rupture is most often spontaneous and bears no relation to any known factor.

8. Spontaneous subarachnoid hemorrhage due to ruptured aneurysms of the circle of Willis is by no means a rare catastrophe and in our experience about 2 per cent of sudden or unexplained deaths encountered by medical examiners are due to this condition.

After rupture, one half of the patients die within an hour, the rest live but a few hours or days, and only a few live a week or longer.

Most deaths occurred in the third, fifth and sixth decades. The younger individuals usually show no atheroma or evidence of syphilis. The older cases often reveal the ordinary amount of arteriosclerosis which is compatible with the age of the individual.

10. There is no effective treatment for this catastrophe. There are no means of prevention, since the aneurysmal fault is usually congenital. The condition is unpredictable, cannot be prevented, and little hope can be offered at this time for any rapid advance in diagnosis or treatment.

11. Since in spontaneous subarachnoid hemorrhage the very character of the

onset is frequently in the nature of an accident, and is often associated with a fall or other injury, it must be differentiated from various cranial injuries and types of intracranial hemorrhage. Traumatic and neurosurgeons should, therefore, be familiar with this condition.

REFERENCES

1. Ayer, Wardner D. So-called spontaneous subarachnoid hemorrhage. *Am. J. Surg.*, 26: 143, 1934.
2. Bramwell, Edwin. Spontaneous subarachnoid hemorrhage. *Brit. M. J.*, 2: 512 (Sept. 14) 1935.
3. Boyd, William. A Text Book of Pathology. Phila., 1934, Lea & Febiger. Second Edition, page 869.
4. Eppinger, H. Pathogenese der Aneurysmen einschliesslich des Aneurysma equi verminosum; pathologisch anatomische Studien. *Arch. f. klin. Chir.*, 35: 1, 1887.
5. Forbus, W. D. On the origin of miliary aneurysms of the superficial cerebral arteries. *Bull. Johns Hopkins Hosp.*, 47: 239, 1930.
6. Helpern, Milton. Multiple saccular aneurysms of the cerebral arteries. *Proc. New York Path. Soc.*, May 26, 1933.
7. Karmally, Abdulla, and Manohar, K. D. Spontaneous subarachnoid hemorrhage. *Brit. M. J.*, 2: 962 (Nov. 13) 1937.
8. Fearnsides, E. G. Intracranial aneurysms. *Brain*, 39: 224, 1916.
9. Martland, Harrison S. The pathology of syphilis. *Bull. New York Acad. Med.*, 8: 469 (July) 1932.
10. Garvey, P. H. *Arch. Opbth.*, 11: 1032, 1934.
11. Howell, C. M. Hinds cerebral vascular accidents. *Brit. M. J.*, 1: 255 (Feb. 6) 1937.
12. Friedman, E. D. Intracranial Aneurysms. In Cecil, R. Text Book of Medicine. Phila., 1937. Saunders, Fourth Ed., pages 1413 to 1415.
13. Sosman, M. C., and Vogt, E. C. *Am. J. Roentgenol.*, 15: 122, 1926.

Ice tong traction [in fractures of the shaft of the femur] is not without its dangers and should be discarded in favor of Kirschner wire traction.

THE ROLE OF PRELIMINARY MEDICATION IN THE PREVENTION OF ANESTHETIC DEATHS

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IN 1935, Henson[4] reported having sent questionnaires to all the hospitals in New York City, numbering 213, requesting the number of the various anesthetics administered during the five year period 1928 to 1932, inclusive. Fifteen replies were received, involving ether, nitrous oxide, ethylene, spinal, local and avertin.

From the Chief Medical Examiner's Office it was found that 219 deaths were apparently caused by anesthesia. This is an average of forty-three deaths per year, a mortality which appears relatively insignificant when viewed from the standpoint of the number of anesthetics administered, but which appears in a different light on realization of the actual number of persons dying from this cause. These deaths were thought to be true anesthetic deaths, to which no pathologic condition of the patient contributed.

In 1937, after a continuance of the study, involving a larger number of anesthetic agents and combinations thereof, Henson[5] concluded that the two investigations had proved that the average number of deaths due to anesthesia per year in the five boroughs of New York was forty-six.

If it is assumed that a cross section of the country is represented by the findings in New York City hospitals, Dr. Henson's statistics would seem to prove that anesthetic deaths have not decreased notwithstanding the development of new agents and improvements in technique. The problem, then, naturally and logically centers around the determination of an agent or agents to be employed, as well as a method or methods of administration, by which these unnecessary deaths may be reduced to a minimum or prevented altogether.

THE MEDICAL AND NURSE ANESTHETIST

While advocating the training and careful regulation of anesthetists, among other considerations, Henson seems to predicate reduction in anesthetic mortality chiefly on the exclusive use of ethylene, with the necessary precautions, as no deaths were reported in this series from ethylene.

In the discussion of Dr. Henson's first paper, Dr. Paul M. Wood of New York City expressed the view that seldom is the agent any more at fault than the method and skill of the anesthetizer. "Given a properly trained and qualified anesthetist, morbidity and mortality will fall, regardless of agent, technique or patient's condition." This point of view was crystallized by the American College of Surgeons in a statement in its 1936 Year book.[9] The statement in part follows:

"The science of anesthesia is rapidly developing. New types of anesthesia, new methods of administration, and complicated apparatus demand serious medical thought. It is unfortunate that a large number of hospitals fail to recognize the necessity and value of a well organized department of anesthesia. This presupposes competent medical supervision, preferably a medical anesthetist. . . . Such a requirement does not preclude the use of the nurse anesthetist who is properly trained and qualified to give anesthesia. It is unfair to expect the nurse to be responsible for the service, but rather she should work under proper medical supervision. As the administration of anesthesia is generally conceded to be the practice of medicine and inasmuch as it involves risk to human life, it is only reasonable to expect medical supervision. This cannot be done properly

by the surgeon, for he is frequently not specially trained in this work, nor should he have to carry the responsibility when under the strain of operating."

Undoubtedly a great advance toward the reduction of anesthetic mortality and morbidity would be made if all medical colleges and hospitals would place in charge of the teaching of anesthesia and the administration of anesthetics competent medical anesthetists who would initiate such methods as would give the safest and most efficient anesthesia. Under these circumstances the patient and the surgeon would be assured of the use, not only of the agent best suited to the case, but of such adjuvant principles of administration as are known to increase the margin of safety.

COMBINATIONS AND SEQUENCES

In his investigations, Henson has developed more clearly than any other writer that statistically nitrous oxide is a very unsafe anesthetic and that ethylene is an unusually safe agent. Luckhardt[7] demonstrated these facts in the laboratory; clinical history has verified and confirmed his findings that ethylene is safer than nitrous oxide. It is a mistake, however, to use either ethylene or nitrous oxide alone; safety lies in using them in sequence and combination, with a trained anesthetist adjusting the requirement for the given case. The majority of anesthetists prefer to have all known anesthetic agents at their command and to use them as indicated by the condition of the patient and the nature of the surgical operation.

THEORETICAL CONSIDERATIONS

In his second paper, Henson[5] reports a total of sixty-one deaths previous to operation (presumably less than ten minutes before), and thirty-two within approximately ten minutes of the commencement of the operation. This total of ninety-three deaths represents nearly 50 per cent of the entire number of deaths reported with the time of occurrence of death and the agent stated. All or nearly all of these deaths could have been avoided by utilizing technique based on laboratory experiments and clinical observations.

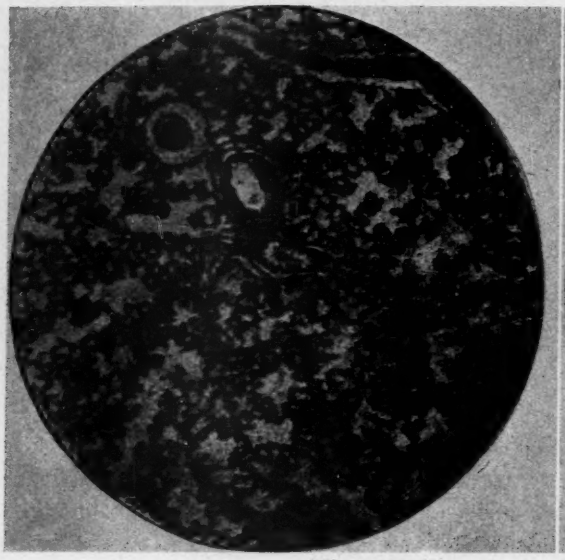
LABORATORY EXPERIMENTS

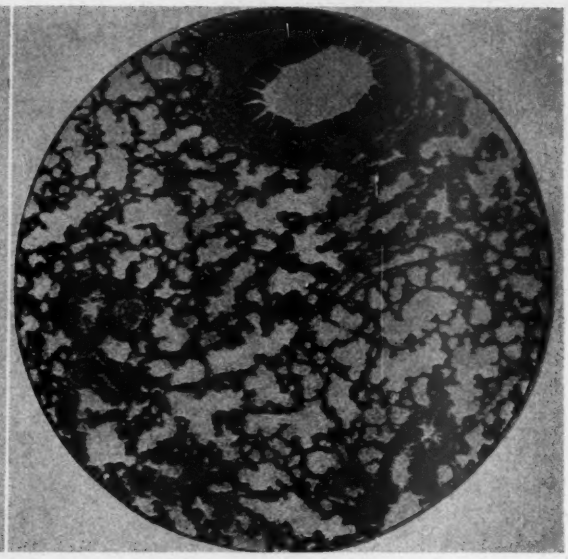
It has been proved experimentally* that when ether is administered intravenously without preliminary medication nearly twice as much anesthetic is required to produce anesthesia as when preliminary medication is used. Again, without preliminary medication a very small amount of ether produces respiratory paralysis, whereas with preliminary medication two and a half times the amount of ether is required to produce this same result. This proves that a laboratory animal is much safer with preliminary medication than without. The above experiment was verified several years later with ether, propylene, acetylene, ethylene, and nitrous oxide administered by inhalation.

This research was under the supervision of the late Charles W. Hooper, assisted by the writer. It represents a year's work, in which approximately 500 animals were employed to determine the value of preliminary medication in inhalation anesthesia. Half of the animals were used as controls and the other half were given preliminary medication; all of them were placed in the same gas chamber. The animals without preliminary medication had a stage of excitement, jumped around and struggled against the anesthetic. The animals with preliminary medication never moved, but sank quickly and quietly under the anesthetic, and lived twice as long as the controls in the same gas chamber. Necropsy revealed that the lungs of the animals that received preliminary medication were relatively normal. The lungs of the animals without preliminary medication on gross examination showed distention, edema and congestion. Microscopic lesions were perivascular edema, diffused

* A protocol of an experiment made in New York University and Bellevue Hospital Medical College by Professor George Barclay Wallace of the Pharmacological Department.

petechiae, and alveolar spaces filled with fluid. The bronchi contained edematous fluid. Other organs appeared normal.

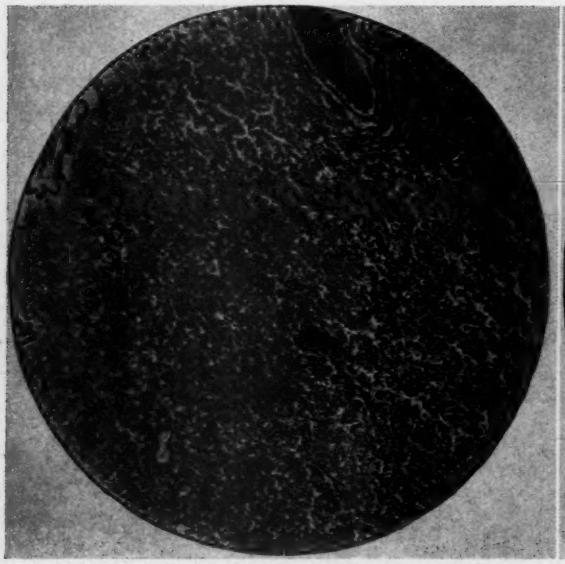


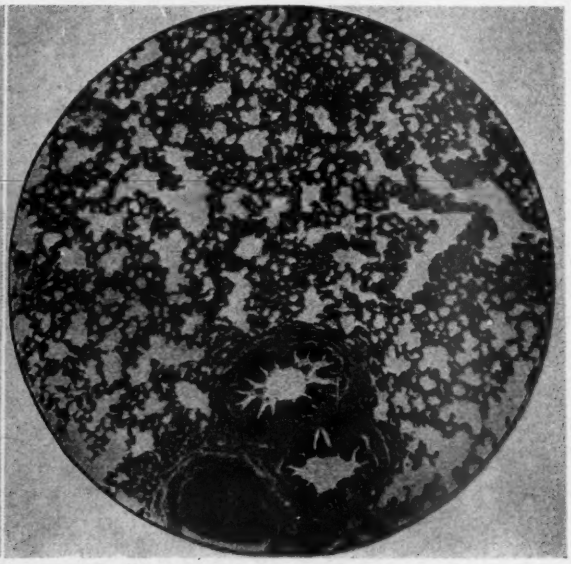


Nitrous oxide 93 per cent, oxygen 7 per cent.

FIG. 1. No preliminary medication. Air spaces filled with edematous fluid; perivascular edema; congestion.

FIG. 2. *Preliminary medication.* Air spaces and bronchi clear; no perivascular edema or congestion.





Ether vapor 34 per cent, oxygen 66 per cent.

FIG. 3. No preliminary medication. Massive atelectasis and congestion; air spaces obliterated.

FIG. 4. *Preliminary medication.* Lung tissue relatively normal.

The work of Charles W. Hooper, assisted by the author. From Autochrome photomicrographs in Nelson's Looseleaf Surgery, Vol. 1, page 514.

PRELIMINARY MEDICATION

As we know, all advanced surgical work is based on laboratory research. Many of the most scientific methods in anesthesia have been evolved from laboratory experiments. Therefore, on the basis of the extensive and careful laboratory experiments with preliminary medication, it is safe to assume that at least 50 per cent of the deaths reported by Dr. Henson as occurring previous to operation and within approximately ten minutes of the commencement

of operation, could have been prevented by the use of preliminary medication.

It has been my experience that preliminary medication is a life-saving measure, some form of which should be employed whenever possible. The ideal preliminary medication has not been found, as such medication should combine within itself the terminal anesthetic. However, the agents or combinations thereof now available which meet certain outstanding requirements (notably elimination of *psychic* reflexes, with the attendant rise in blood pressure) will bring the patient to the state or condition corresponding to that of an animal given preliminary medication in the laboratory, i.e., partial or complete insensibility when brought to the operating table.

Morphine (*¼ grain*) *and atropine* (*1/150 grain*) form an unsatisfactory preliminary medication as they do not abolish the psychic reflexes. A tremendous rise in blood pressure is always present preceding the initiation of the anesthetic.[1]

Several new preliminary medicaments have been introduced within the last few years that have proved satisfactory and entirely safe. Notable among these is nembutal (pentobarbital sodium) and evipal soluble.[3] Whatever the agent, the timing of its administration so that its maximum effect is produced as the patient is brought to the operating table is most important.

Nembutal has been used in over 2,000 consecutive cases of adenoid and tonsil operations in the City Hospital of New York.[2] The children are sound asleep when brought to the operating table. The fright and struggle which usually accompany anesthesia in children who have not received preliminary medication are eliminated. The sleep is converted into surgical anesthesia, carried sufficiently deep to abolish all reflexes, without awakening the patient. As the terminal anesthetic does not have to be pushed, the throat reflex returns before the child leaves the operating table. This is an ideal technique for the removal of adenoids and tonsils in children. Nembutal in proper dosage, also gives satisfactory results in adults.[8]

Evipal soluble administered *rectally* has proved safe and most satisfactory in producing quiet sleep in adults. This preliminary medication may be supplemented by the rectal administration of one or two ounces of ether and an equal amount of oil. It is usual to supplement this in the operating room by ethylene and oxygen, or ether and oxygen. For prolonged operations, plastic or brain surgery, nothing is more satisfactory than ether and oil by rectum, supplemented *intermittently* by small amounts of anesthetics by inhalation when necessary.

The idiosyncrasies that sometimes appear following the administration of local and spinal anesthetics will be suppressed or very greatly diminished by the administration of some barbiturate as a preliminary medicament in local, spinal, or inhalation anesthesia. Evipal soluble by rectum is recommended as perfectly safe, since the difference between the anesthetic and the toxic dose in this method is 4 plus or greater than any anesthetic agent or method in general use today.

"*Lathesia.*" The most recently employed preliminary medication is a mixture of ether in pure caoutchouc. This combination reduces by less than one-half the bulk usual with equal amounts of ether and oil. It is similar to vaseline, but more liquid, and comes readily prepared in desired amounts in collapsible tubes with rectal adapters. The tubes and adapters are thrown away after use. The material is stable, the latex acting as a stabilizer and anti-oxidant.

In the pharmacologic laboratories of New York University Dental School, Professor Neuwrith, parallelling the experiments of the late Professor Charles Baskerville,[11] proved by laboratory experiments that ether evaporates from "lathesia" evenly, as it does from oil, at body temperature. Clinically, it apparently acts in the same manner as does the ether and oil mixture. It is much easier to give and much

CHART I
(By E. R. Plumb, Anesthetist)

Operation June 1937	Age	Wt.	1½ Hours Preop. Hypo.	1¼ Hours Preop. Amount Rectal Evipal	Sleeping after Evipal	1 Hour Preop. Amount Rectal Lathesia	Terminal Anesthesia	Blood Pressure		Relaxation	Postop. Nausea	Remarks
								Pre-op.	Post-op.			
Repair of rectocele and cystocele	47	117	Magendie m. 7	3 Gm.	8 min.	0	$C_2H_4 + O_2$	148/94	140/80	Satisfactory	None	Reacted in 1½ hours. Metrazol 2 c.c.
Hysterectomy	47	170	"	3 Gm.	4 min.	℥ ii	None	128/88	120/84	Excellent	None	Reacted quietly in 4 hours. Metrazol 2 c.c. Resp. 8–12 during op.
Appendectomy, uterine suspension, bilateral salpingectomy	28	170	"	3 Gm.	5 min.	℥ ii	$C_2H_4 + O_2$ for closing of abdomen	138/98	128/90	Excellent	None	Op. postponed 1 hour, 40 minutes. Reacted 3½ hours quietly. Metrazol 2 c.c.
Appendectomy	26	133	"	2 Gm.	12 min.	℥ i	$C_2H_4 + O_2$	128/88	120/84	Excellent	None	Reacted quietly 2 hours. (?) Metrazol 2 c.c.
Resection of portion left ovary, appendectomy	50	136	"	2 Gm.	8 min.	℥ i	$C_2H_4 + O_2$	145/95	140/100	Excellent	None	Reacted quietly 5 hours. (?) Metrazol 2 c.c.
Resection of parotid cyst	59	148	"	0	0	℥ v	$C_2H_4 + O_2$ for a few minutes to control cough reflex	168/110	168/110	Excellent	None	Reacted quietly 1½ hour
Repair of rectocele and cystocele	54	160	"	3 Gm.	10 min.	0	$C_2H_4 + O_2$	128/88	136/90	Satisfactory	None	Reacted quietly Time (?) Metrazol 2 c.c.
Hysterectomy, excision of ovarian cyst	49	164	"	3 Gm.	4 min.	℥ i	$C_2H_4 + O_2$	124/88	120/80	Excellent	None	Reacted quietly 45 min. postoperatively. Metrazol 2 c.c.
Hysterectomy	48	138	"	2 Gm +	8 min.	℥ ii	None	118/78	124/80	Very good	Vomited once	Reacted quietly 2 hours 15 minutes. Metrazol 2 c.c.
Ventral suspension, appendectomy	34	132	"	2 Gm.	11 min.	℥ ii	$C_2H_4 + O_2$	128/74	120/80	Very good	None	Reacted quietly 2 hours 45 minutes. Metrazol 2 c.c.
Excision ovarian tumor March '37	37	128	"	2 Gm.	12 min.	℥ i	$C_2H_4 + O_2$ + Ether	104/60	112/68	Very good	None	Reacted quietly. Time?
Uterine suspension March '37	28	120	"	2 Gm.	8 min.	℥ i	$C_2H_4 + O_2$	118/80	124/80	Very good	None	Reacted quietly. 25 minutes.
Vaginal plastic March '37	39	140	"	3 Gm.	6 min.	0	$C_2H_4 + O_2$	104/58	100/60	Very good	None	Metrazol 3 c.c. Reacting at end of operation
Sturmdorf operation March '37	40	136	"	3 Gm.	4 min.	0	$C_2H_4 + O_2$	148/100	140/92	Very good	None	Metrazol 3 c.c. Reacted quietly. Time?
Lorenz bifurcation	70	120 ?	Magendie sol. m. 5	1.5 Gm.	10 min.	0	$C_2H_4 + O_2$	140/88	132/90	Very good	None	Reacted in op. room

These cases do not always follow the above schedule as to time evipal and premedication were given, but where it is possible to do so they are kept to this schedule. Metrazol 3 c.c. is now used routinely. E. R. Plumb, Anesthetist.

more pleasant for the patient to take the same amount of ether in "lathesia" than when mixed with oil. The latex is in no way altered by the body chemistry or temperature and is considerably less expensive than the full oil-ether mixture. In the large quantities used, this means a saving of thousands of dollars. Latex is not absorbed, but is expelled by the next bowel movement. Chart 1 gives for the first time a report of the use of "lathesia" in surgical operations. As ether per rectum practically eliminates nausea and vomiting, this new method of administration will greatly popularize ether as a therapeutic measure in whooping cough and other diseases, as a supplement to rectal evipal and avertin, or as a preliminary or complete anesthetic.

SUMMARY

It is now a common practice in some clinics to give oil-ether, evipal, nembutal, avertin, or some other drug in order to avoid the possibility of lung lesions and psychic reflexes and the unpleasant experiences usual with a patient anticipating and dreading the unknown, regardless of the terminal anesthetic or method of administration.

Both morbidity and mortality can be decreased by the universal use of a safe preliminary medication. Preliminary medication is practically synonymous with safety to life in anesthesia.

The 120 deaths listed by Dr. Henson as occurring within an hour or so after the induction of anesthesia would be prevented when and if the suggestion of the American College of Surgeons is accepted by hospitals and medical colleges.

"Ether" deaths are unnecessary, and simply mean that internes without adequate knowledge or instruction are giving anesthetics as one of their first duties on or before leaving college. Albert Miller[10] has shown that ether is safer than nitrous oxide as regards both morbidity and mortality *when the anesthesia is in the hands of qualified anesthetists.*

Experience has proved that when a patient is returned to bed, asleep after an operation, he should be turned from side to side every hour in order to secure free ventilation of the lungs. An airway tube should be left in situ until the reflexes return.

Nearly all anesthetic deaths, as such, are avoidable, provided the anesthetist is properly trained and has the necessary equipment.

REFERENCES

1. Coburn, R. C. Blood pressure in operative surgery and general anesthesia. *J. A. M. A.*, 82: 1748–1750 (May 31) 1924.
2. Gwathmey, J. T. Premedication and inhalation anesthesia for tonsil and adenoid operations in young children. A humane and safe method. *Am. J. Surg.*, 31: 272–274 (Feb.) 1936.
3. Gwathmey, J. T. Rectal administration of evipal soluble; a safe, reversible and controllable preanesthetic medication; a preliminary report. *Am. J. Surg.*, 32: 411–416 (June) 1936.
4. Henson, C. W. A review of established anesthetics. With analysis of deaths in New York City for five year period. *New York J. Med.*, 36: 485–490 (April) 1936.
5. Henson, C. W. The relative safety of anesthetics. In press.
6. Hooper, C. W., and Gwathmey, J. T. Preliminary medication in general anesthesia; with special reference to the margin of safety and postoperative lung lesions. *Current Res. Anesth. & Analg.*, 7: 167–169 (May–June) 1928.
7. Luckhardt, A. B., and Carter, J. B. The physiologic effects of ethylene; a new gas anesthetic. *J. A. M. A.*, 80: 765–770 (March 17) 1923.
8. Lundy, J. S. Experiences with sodium ethyl (1-methylbutyl) barbiturate in more than 2300 cases. *S. Clin. North America*, 11: 909–915 (Aug.) 1931.
9. MacEachern, M. T., and Williamson, E. W. Hospital Standardization. American College of Surgeons, Twenty-third Yearbook, 1936, page 71.
10. Miller, A. H. Fiske Fund Prize Essay, No. LXVI; Anesthetics, their relative values and dangers. *Rhode Island M. J.*, (supp.) pp. 1–51 (Sept.) 1931.
11. Baskerville, Chas. *J. Indus. & Engin. Chem.*, 7: 868–870, 1915.
12. Jones, A. E. *J. A. M. A.*, 110: 1419–1423 (April 30) 1938.

APNEA DURING ANESTHESIA*

THE RELIEF OF ANOXEMIA AS A POSSIBLE CAUSE

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IT is generally stated that under physiologic conditions apnea is largely due to excessive elimination of carbon dioxide from the blood. That other factors are concerned in the control of respiratory activity is well established. Afferent impulses from various parts of the body influence the activity of the respiratory center. Reflexes from the lungs stimulated by respiratory movements and those arising from the carotids and aorta due to changes in the chemical composition of blood are essential to respiratory control.

During anesthesia normal physiologic conditions of respiration are always disturbed. The physical condition of the patient that prompts surgical intervention is frequently a factor and the depressant drugs used for anesthesia as well as the technique by which they are employed always contribute to the alteration. Not infrequently the derangement of normal function is manifested by a depression of the activity of the respiratory center to the extent that respiratory movements cease or apnea results. In the advent of such apnea it is extremely difficult to assess the influence of the various factors that may be involved, and consequently, it is perplexing for the anesthetist to decide upon the proper procedure to prevent deleterious results. If the apnea is attributed to excessive elimination of carbon dioxide from the blood and treatment is attempted by forcing carbon dioxide into the lungs, serious consequences will frequently follow. However, if treatment of apnea is based upon the known fact that the accompanying anoxemia will in a very short time damage the heart and brain, then oxygen will be forced into the lungs and the possibilities of unfavorable results are minimized.

During clinical anesthesia, phenomena may be observed which lead to the deduction that increasing the oxygen tension of the inspired atmosphere depresses respiration or causes apnea. Specific examples of some such incidents are cited, together with a brief discussion of the possible mechanism involved. It is our purpose to point out that such apneas are due to an error in anesthetic technique. Although the oxygen concentration of the inspired atmosphere is increased at the time apnea occurs, the treatment includes maintaining a relatively high alveolar oxygen tension.

CASE 1. J. S., male, aged 40. Operation: Sacroperineal resection of rectum. Preanesthetic medication: morphine sulphate gr. $\frac{1}{4}$ (0.016 Gm.) and scopolamine gr. $\frac{1}{150}$ (0.00048 Gm.) administered subcutaneously.

Anesthesia was begun one and one-half hours later with cyclopropane, using a closed system with a unit to absorb carbon dioxide. Approximately 1,500 c.c. of oxygen was introduced into the breathing bag, then cyclopropane was added at a rate of 500 c.c. per minute, together with 1,200 c.c. of oxygen per minute. After three minutes, cyclopropane was discontinued and the oxygen flow maintained at 400 c.c. per minute. Two minutes later, respirations ceased. The pulse was found to have diminished in rate from 100 to 60 beats per minute and the blood pressure recorded a slight change from 110/70 to 100/60. Apnea persisted for three minutes until the anesthetic mixture in the rebreathing

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bag was partially replaced by nitrous oxide and introduced into the lungs by positive pressure. Breathing then resumed at a rate of 20 respirations per minute, but the patient was slightly cyanotic. The sudden introduction of a blast of oxygen in the anesthetic mixture resulted in respiratory arrest lasting four minutes or until relieved by the administration of nitrous oxide. Apnea occurred again fourteen minutes later and an attempt to correct it by removing the canister of soda lime from the system for five minutes, with consequent increase in the carbon dioxide concentration, was futile. When the oxygen concentration was reduced, spontaneous respirations were immediately restored and maintained at the expense of evident subcyanosis. Twenty minutes later apnea was again demonstrated. The anesthetic mixture in the breathing bag was eliminated and a mixture of 1,000 c.c. of oxygen with 200 c.c. of cyclopropane flowing per minute was administered for two minutes, whereupon respiration ceased. Spontaneous breathing was not resumed until the oxygen concentration was reduced by addition of nitrous oxide.

At the end of the operation, when the anesthetic apparatus was removed, pure oxygen was added to the inspired atmosphere by holding a rubber delivery tube with oxygen flowing 8 to 10 liters per minute, over the patient's nose and mouth for several seconds and this once more caused an apnea of two minutes' duration.

Case II. J. M., male, aged 28, suffering from tuberculous peritonitis, was scheduled for exploratory laparotomy. Preanesthetic medication, consisting of morphine sulphate gr. $\frac{1}{6}$ (0.010 Gm.) and scopolamine gr. $\frac{1}{150}$ (0.00048 Gm.), was administered at 10:30 A.M. and repeated, by error, at 11:00 A.M.

At 11:45, anesthesia was induced with cyclopropane and oxygen. After several breaths apnea occurred. Artificial respiration by pressure on the breathing bag was begun and maintained. After fourteen minutes spontaneous respirations returned, first at a rate of six per minute but gradually increasing in frequency during the next half hour until they reached twenty per minute when the operation was completed. Blood pressure and pulse alterations were insignificant throughout the operation. First plane surgical anesthesia was maintained with satisfactory abdominal relaxation.

Case III. J. A., a boy of 7 from the tuberculosis service, developed acute appendicitis. Appendicectomy was urgently proposed. Morphine sulphate gr. $\frac{1}{10}$ (0.006 Gm.) and atropine sulphate gr. $\frac{1}{300}$ (0.00024 Gm.) were administered for preanesthetic medication at 12:45 P.M., and because of an error the same amount was given at 1:30 P.M. The child received a total of morphine sulphate gr. $\frac{1}{5}$ (0.012 G.) and atropine sulphate gr. $\frac{1}{150}$ (0.00048 Gm.).

Induction of anesthesia was accomplished, using cyclopropane with a high oxygen dilution by the carbon dioxide absorption technique. At the end of two minutes the patient's respirations ceased. Artificial respiration was instituted, but after five minutes apnea still persisted. The carbon dioxide absorber was then removed from the rebreathing system and artificial respiration continued for five minutes allowing carbon dioxide to accumulate in the rebreathed mixture. Spontaneous respirations did not occur. The pulse rate and rhythm were little changed and active eyeball motility established the degree of narcosis in light surgical plane. At 2:35 P.M., 1.5 c.c. of metrazol was injected subcutaneously and artificial respiration continued. At 2:45 the patient reacted, opened his eyes, moved his head and breathed spontaneously at a rate of twenty per minute. Cyclopropane with excess oxygen was reintroduced and five minutes later apnea occurred again for four minutes. Breathing then resumed, at first shallow, at a rate of ten respirations per minute, gradually becoming deeper, and finally reaching a rate of twenty-two per minute at the end of operation.

Case IV. L. R., male, aged 74, was scheduled to have a suprapubic cystostomy. Morphine sulphate gr. $\frac{1}{6}$ (0.010 Gm.) and scopolamine hydrobromide gr. $\frac{1}{150}$ (0.00048 Gm.) were administered at 12:40 P.M. At 2:00 P.M., upon arrival at the operating room, the patient was markedly depressed, as evidenced by stupor, pin-point pupils, and sub-cyanosis. He reacted sluggishly to pain and to loudly spoken questions. Respiration appeared normal at a rate of twenty-two per minute, of fair amplitude, with intercostal and abdominal activity both present. The pulse rate was 108. Infiltration anesthesia was used. Before operation pure oxygen was administered in a closed system with the carbon dioxide absorber in place. The patient's color rapidly improved and the pulse

rate slowed to 100. Respirations became decidedly shallower and intercostal activity was lost although the rate changed only from twenty-two to twenty per minute. This status was maintained for five minutes. Upon discontinuing the oxygen, respirations deepened, the rate increased to twenty-four per minute and intercostal muscles became active. The pulse rate returned to 108 and subcyanosis recurred. The operation was then quickly performed under local anesthesia.

At its conclusion the patient was still stuperous. Metrazol 1.5 c.c., injected intravenously with a similar amount intramuscularly, elicited an immediate response. The patient became more alert and could understand spoken questions. In bed ten minutes later, the patient was in a state of tonic contracture with occasional generalized tremors. Nasal oxygen and an intravenous infusion were started. At 5:00 P.M., he was irrational and apprehensive, necessitating restraint. At 10:00 P.M. he was still restless and mentally confused. Oxygen therapy was continued during the night. In the morning the patient seemed normal, cheerful and coöperative. Recovery was progressive without evidence of any effect from the experience.

Three cases are here reviewed in which patients received excessive premedication with morphine and scopolamine or atropine, and exhibited apnea during cyclopropane anesthesia. During cyclopropane anesthesia with the technique in use here, the concentration of oxygen in the alveolar air is more than 30 per cent.[1] These apneas were not due to an anesthetic overdose, since in the first case spontaneous respiration was restored by the administration of nitrous oxide. Artificial respiration with pure oxygen for several minutes did not relieve the apnea. The apnea was not due to acapnia since it could be produced without carbon dioxide absorption, that is, by using a closed rebreathing system for five or more minutes so that the carbon dioxide content was increased by accumulation of the carbon dioxide exhaled. Since the return of spontaneous respiration following the administration of nitrous oxide was always accompanied by cyanosis and since attempt to relieve this cyanosis by increasing the oxygen content resulted in respiratory arrest it was evident that respiratory activity in these cases was, in a large part at least, dependent upon some degree of anoxemia. Similar reactions are observed under nitrous oxide anesthesia where suddenly increasing the oxygen after marked cyanosis has developed frequently results in short periods of apnea.[2] Another case (IV) demonstrates that when morphine is given in a quantity sufficient to cause stupor and sub-cyanosis, the inhalation of atmospheres rich in oxygen may cause further depression of respiration, as evidenced by a decrease in respiratory amplitude and by a loss of intercostal activity in one subject.

In the experimental animal the mechanism for the production of this oxygen depression has been demonstrated.[3,4] When morphine and barbiturates are given, alone or combined, in doses sufficient to cause respiratory depression and anoxemia, the administration of oxygen results in increased respiratory depression or apnea and respiratory failure. The addition of 5 to 10 per cent carbon dioxide to the inspired atmosphere does not prevent this phenomenon. It has been shown that the animals receiving large doses of barbituric acid derivatives and morphine maintained respiration by an anoxemic stimulus acting through the sino-aortic mechanism and that the administration of oxygen which relieved anoxemia resulted in hypopnea or even apnea.[4]

Similar results have been noted in rats where cyanosis and asphyxial symptoms occurred following the injection of large doses of sodium iso-amyl ethyl thiobarbiturate. In such cases, the animals treated with oxygen two to five minutes after the appearance of respiratory difficulty recovered, but those in which cyanosis and dyspnea had persisted for more than a half hour, oxygen inhalation resulted in shallower respiration followed by periods of apnea and finally death.[5] In the dog, reactions similar to those observed in the first two clinical cases have been recorded here. Animals were premedicated heavily with morphine and

atropine, then anesthetized by cyclopropane and oxygen, using the carbon dioxide absorption technique. Shortly after anesthesia was established respirations would cease. This apnea could be immediately relieved by the addition of nitrous oxide or nitrogen sufficient to cause cyanosis and again reproduced by adding oxygen.

When the respiratory center is depressed the hypoxemia which follows is an effective stimulus to receptors in the carotid body which in turn stimulate respiration and increase pulmonary ventilation.[6] This anoxemic hyperpnea is mainly or entirely reflex and should not be confused with the hyperpnea of carbon dioxide and acid excess which is more central than reflex. In contrast to this reaction in the intact animal, in those with the vagi divided and the carotid sinus denervated anoxia causes depression of respiration.[7] Although there is clinical and laboratory evidence to show that oxygen may produce respiratory depression, it is not oxygen in itself that causes this phenomenon. It is due to excessive use of depressant drugs for preanesthetic medication and anesthesia. These inhibit the activity of the respiratory center which is much more sensitive to their depressant effects than is the reflex mechanism arising in the carotid body. Oxygen lack is the only effective stimulus to the carotid body receptors and when it is removed by the inhalation of oxygen at a time when the center is depressed, apnea or depression of respiration will result.

From the practical viewpoint, the treatment of this type of respiratory depression is important. Prophylaxis primes all and the importance of avoiding a combination of drugs that lead to severe depression, cannot be over-emphasized. In this regard, it should be remembered that anesthetic agents are central depressants. Greater depression may be anticipated with the more potent agent and consequently, when they are employed, less preoperative sedation is advised. With cyclopropane, a potent anesthetic gas which does not stimulate but frequently depresses respirations, one-half the usual morphine premedication has been recommended.

Also the relation between preanesthetic medication and the metabolic activity of the patient should be well considered. When a patient, inadvertently over-premedicated, manifests respiratory arrest under anesthesia in which the oxygen concentration is greater than in the normal atmosphere, the correction of this condition should aim at overcoming the cause of the disturbance, namely, the depressed respiratory center and the anoxia.

It should be remembered that depression of the respiratory center by anesthetic drugs is aggravated by a poor supply of oxygen. Any reduction in the oxygen content of the breathing system until spontaneous respiration is reëstablished while cyanosis appears is unphysiologic and adds further damage to the brain and heart. It may, in a very short time, produce permanent cerebral damage through prolonged oxygen lack.[8] In the cases described, nitrous oxide was not employed as a desirable remedy, but rather to demonstrate that respiration was induced by anoxemia. When it is determined that respiration ceases upon increasing the oxygen content and reappears under cyanosis, it should indicate that the respiratory center is inefficient. Rather than to continue this vicious circle, effort should be maintained to overcome this depressive state by persisting in the administration of oxygen together with artificial respiration until the respiratory center regains its normal activity. Case II illustrates the effectiveness of this principle.

The use of carbon dioxide is especially to be condemned. When the respiratory center is severely depressed, increasing the carbon dioxide tension in the inspired atmosphere will usually cause further depression or failure of respiration. If the concentration of carbon dioxide added is excessive it may increase the depression from its own anesthetic action.[9] If some stimulation results from carbon dioxide, it serves only to increase the cell oxygen

requirements and unless oxygen is also increased, a bad situation is made worse.

Central respiratory stimulants may possibly be used with advantage in conjunction with oxygen treatment and artificial respiration. During depression due to morphine overdosage pentamethylene tetrazol (metrazol) is often of value as an analeptic.[10] It may be employed postoperatively when it is observed that, due to the morphine, recovery from anesthesia is unusually prolonged. It may be administered during the course of anesthesia or preoperatively when central nervous depression from preanesthetic medication is evident. Analeptic therapy does not preclude oxygen therapy with which it should always be combined. This is well illustrated in the last case where the respiratory and cerebral stimulation produced by metrazol did not prevent the development of anoxemic symptoms (generalized tremors, irrationality, apprehension and restlessness) which diminished and disappeared following prolonged oxygen administration.

Case IV also emphasizes the importance of early and prolonged treatment. When drugs have been administered that depress the respiratory center to the extent that respirations are carried on mainly by an anoxemic stimulus to the carotid body, treatment is urgently indicated. The administration of oxygen should not be delayed until inhalation anesthesia is inaugurated. It is equally important that treatment be continued after surgery is completed.

SUMMARY

1. Observations of clinical cases are presented which corroborate the experimental findings that when central respiratory depression and anoxemia are present the administration of oxygen may further depress respiration to the point of respiratory arrest.

2. When the two conditions, depressed respiratory center and anoxemia, exist, respiration is carried on mainly by an "anoxemic stimulus" mediated through the carotid body.

3. Morphine medication is a frequent factor in causing central respiratory depression with ensuing hypoxemia resulting in respiratory activity maintained by an "anoxemic stimulus." Further addition of an anesthetic agent enhances the central depression so that the administration of high concentrations of oxygen may produce apnea by removal of the "anoxemic stimulus."

4. To avoid such apnea during anesthesia, it is recommended that preanesthetic morphine be reduced when a potent non-irritating anesthetic agent like cyclopropane and excess oxygen is to be used.

5. When such apnea does occur it is suggested to maintain high oxygen concentration and employ artificial respiration until spontaneous respiration is resumed. During such apnea the use of carbon dioxide is not advised. A central respiratory stimulant, such as metrazol, may be useful in conjunction with oxygen therapy.

6. When respiratory activity is maintained largely by an anoxemic stimulus by way of the carotid body, treatment with oxygen is indicated to prevent cerebral damage from oxygen want.

REFERENCES

1. Waters, R. M., and Schmidt, E. R. Cyclopropane anesthesia. *J. A. M. A.*, 103: 975, 1934.
2. McKesson, E. I. Nitrous oxide anesthesia for unusual operations. *Anes. & Anal.*, 7: 268 (June) 1928.
3. Stella, G. Respiratory failure following denervation of the carotid sinus. *J. Physiol.*, 87: 488, 1936.
4. Marshall, E. K., and Rosenfeld, M. Depression of respiration by oxygen. *J. Pharmacol. & Exper. Therap.*, 57: 437, 1926.
5. Burstein, C. L., and Rovenstine, E. A. Anesthetic efficiency of sodium iso-amyl ethyl thiobarbiturates. *Anes. & Anal.*, 17: 195 (July) 1938.
6. Schmidt, C. F. Recent studies on some physiological phenomena related to anesthesia. *Anes. & Anal.*, 17: 24, 1938.
7. Heymans, Bouckaert, and Regniers. Le sinus carotidien. Paris, 1933. G. Doin et Cie.
8. Courville, C. B. Asphyxia as a consequence of nitrous oxide anesthesia. *Medicine*, 15: 129, 1936.
9. Leake, C. D., and Waters, R. M. Anesthetic properties of carbon dioxide. *Anes. & Anal.*, 8: 17 (Jan.) 1929.
10. Burstein, C. L., and Rovenstine, E. A. Clinical experiences with newer analeptics. *Anes. & Anal.*, 16: 151, 1937.

FRACTURES OF THE HUMERUS*

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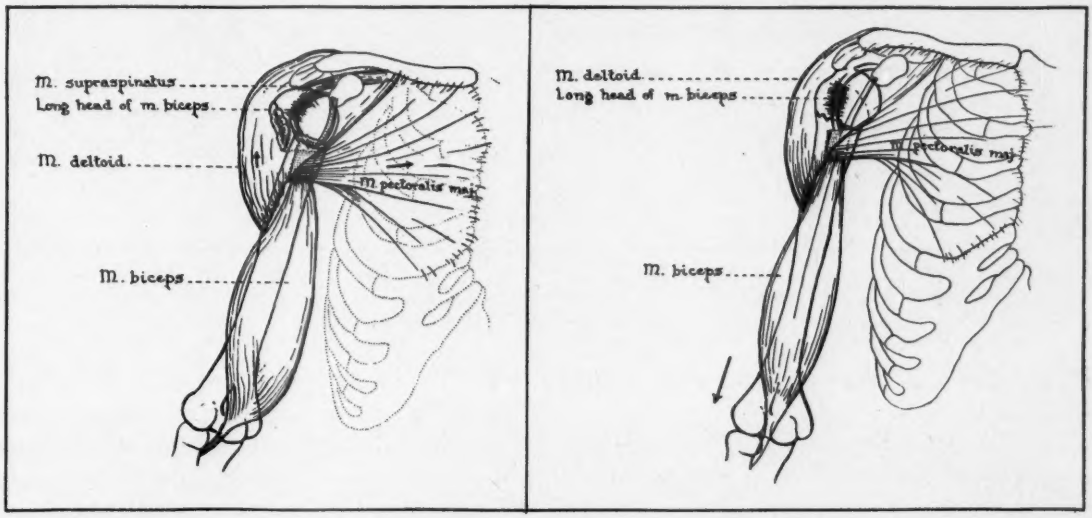
THE treatment of fractures of the humerus entails difficulties which are well recognized. Most of the standard texts present several methods of treatment for each variety of fracture, a lack of unanimity which testifies to the absence of a uniformly satisfactory procedure. Reduction of the fracture is usually not difficult, but satisfactory maintenance of position is often a problem. It is the purpose of this paper to present, or rather to restate, a method of fixation by traction which has proved successful in a large series of cases. With a few rare exceptions, the method is applicable to all varieties of fracture of the humerus. The advantages claimed are: (1) simplicity; (2) comfort; (3) universal applicability to all patients who can assume the erect position; and (4) anatomic and functional results superior to those obtained by other methods or combinations of methods.



A B

FIG. 1. A, the forces causing displacement in fractures above the pectoralis. The head is controlled chiefly by the supraspinatus, which is the most powerful muscle attached to it. The distal fragment is pulled inward by the pectoralis and upward by the deltoid and longitudinal muscles. The long tendon of the biceps lies loose in the bicipital tunnel. B, the result of traction parallel with the body. The taut biceps tendon rolls the head into position, and holds it there.

The fundamentals involved are not new, but have been submerged in a flood of abduction plaster casts, aeroplane splints and intricate procedures for recumbent traction or internal fixation. In principle the method converts the forearm into a lever with the fulcrum at the wrist and force exerted in the line of the humerus. To accomplish this end, the wrist is supported by a sling, and a plaster cast maintains the elbow at a right angle. The cast, plus the unsupported portion of the arm and the forearm, supplies the necessary traction weight. (Fig. 4.) Many of the older texts illustrate this principle with drawings showing the wrist supported

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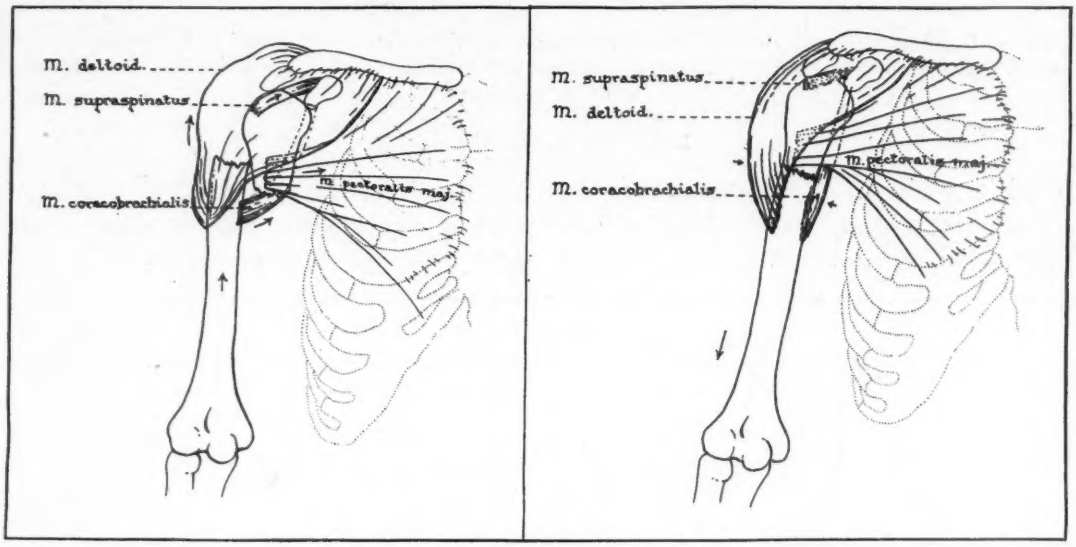
by a sling, and traction applied by a weight suspended from the elbow. Caldwell[1] introduced the plaster cast to supply traction and to control the elbow and distal fragment.



A B

Fig. 2. A, typical displacement in fracture between the pectoralis and deltoid. B, the effect of traction. Tension on the longitudinal muscles results in a squeezing effect at the fracture site.

For purposes of treatment, fractures of the humerus may be divided as follows:

1. Those above the insertion of the pectoralis major.
   (a) Fractures of the head and tuberosities.
   (b) Fractures of the surgical neck.
2. Fractures of the shaft.
   (a) Fractures between the insertions of the pectoralis and the deltoid.
   (b) Fractures of the shaft below the deltoid.
3. Supracondylar and condylar.

Slight variation in details of treatment must be made for each class.

Fractures above the Insertion of the Pectoralis Major. In these fractures the short upper fragment is controlled by the muscles attached to it. The most usual displacement of this fragment is flexion and rotation. Abduction of the short fragment is not so commonly encountered as the wide preference for treatment in abduction would indicate. The shaft fragment is most often displaced anteriorly and drawn medially by the pectoralis. (Fig. 1A.)

The old dictum that the distal fragment must be placed in line with the proximal one may be disregarded. The only reason for this rule is that the proximal fragment is supposedly not under our control. Howard and Eloesser[2] have shown that the intact long tendon of the biceps gives adequate control of the short fragment when traction is applied parallel to the body. This tendon, lying in the tunnel formed by the bicipital groove and its fibrous covering, swings the head into position parallel with the body, correcting abduction and flexion or extension. Rotation is taken care of by the tendon and by placing the forearm across the body. (Fig. 1B.) Traction parallel to the body requires much less pull to maintain reduction than traction in abduction. In the abducted position most of the traction force is wasted in pulling against the powerful pectoralis major, teres major and latissimus dorsi. Three or 4 pounds in adduction is the equivalent of 15 or 20 pounds in abduction.

Reduction of the fracture is carried out under local or general anesthesia by the maneuver of Cotton and Morrison[3] or

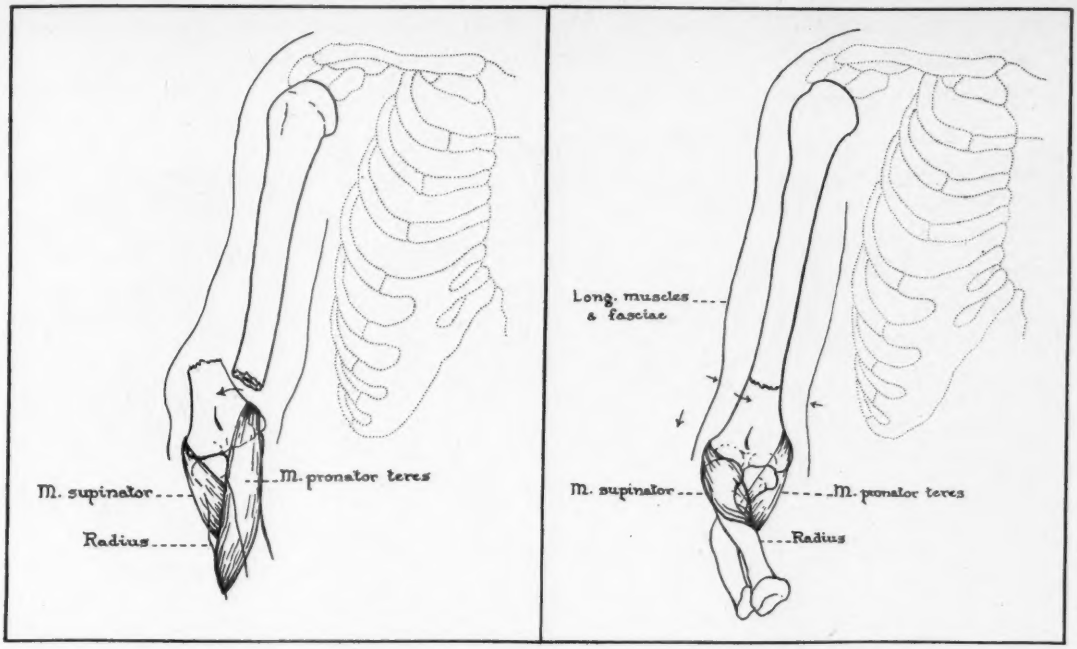


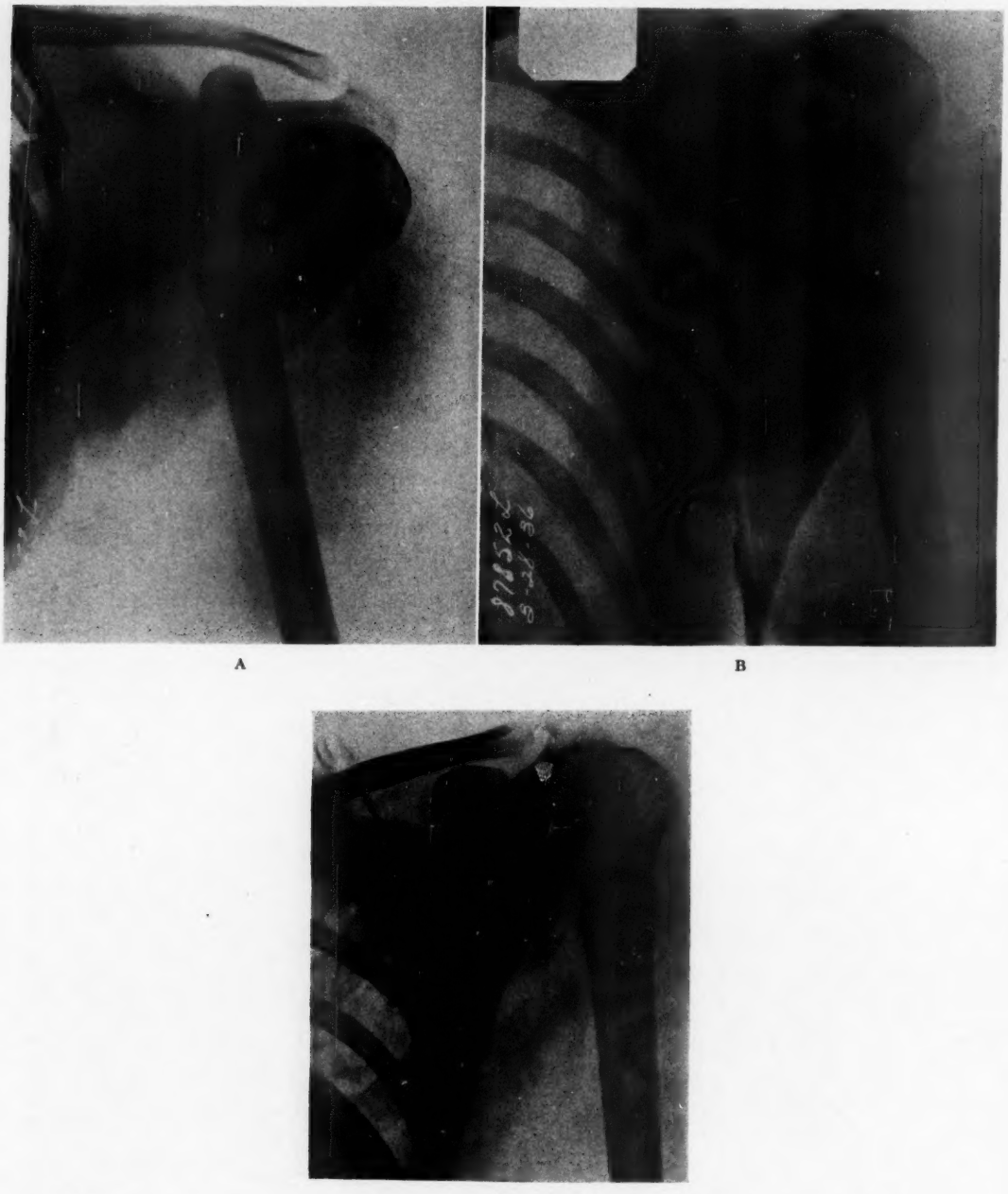
FIG. 3. A, varus deformity in supracondylar and low shaft fractures. Since the elbow is fixed in full pronation, supination (varus) occurs at the fracture site, not at the fixed elbow. B, full pronation swings the distal fragment into correct alignment. Longitudinal muscles and fascia, pulled taut by traction, exert squeezing pressure on the fracture.

FIG. 4. The traction cast in place. Note the right angle at the elbow and the horizontal position of the forearm. The cast extends over the metacarpals to prevent wrist drop.

FIG. 5. The position assumed for circumduction exercise of the shoulder. The arm swings free and is actively moved from the shoulder in all directions.

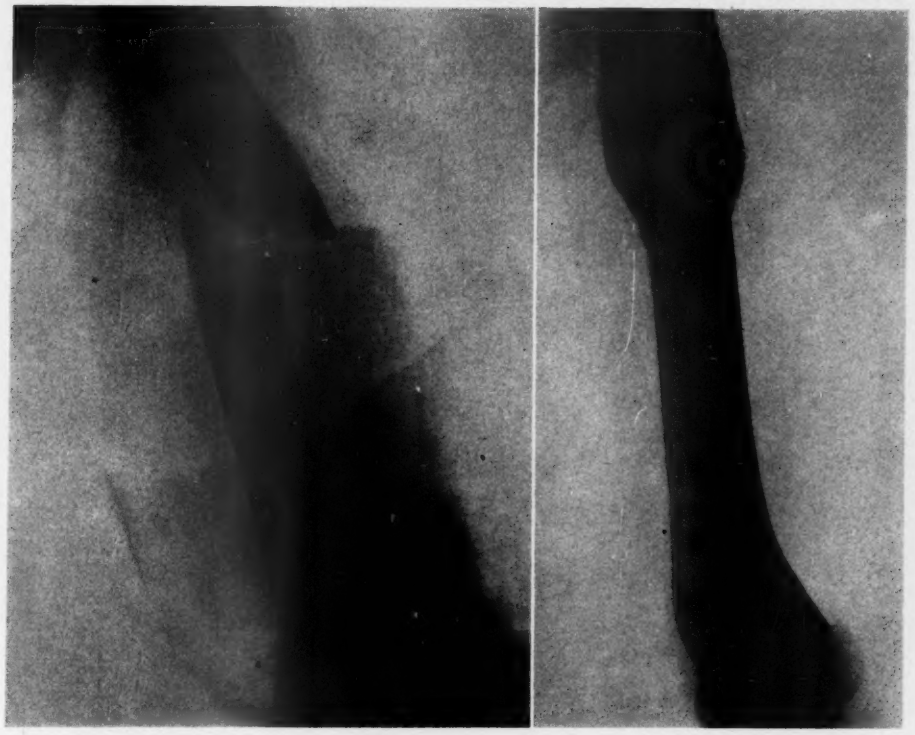
by that of Howard and Eloesser.[2] We prefer the former. A traction cast of 3 to 4 pounds in weight is applied immediately with the elbow at a right angle and the forearm in mid-pronation. In the rare case with rupture of the long head of the biceps, these maneuvers will fail to reduce the fracture, and open reduction with suture of the tendon or fixation of the head[4] are then the methods of choice.

Fractures of the Shaft. Fractures in the small space between the pectoralis and the deltoid are rare. The proximal fragment is usually pulled medially by the pectoralis and the distal fragment upward and outward by the deltoid.



A B C

FIG. 6. A, typical fracture above the pectoralis (patient supine). B, immediately after reduction and application of cast (patient erect). C, the same fracture at the end of two months.



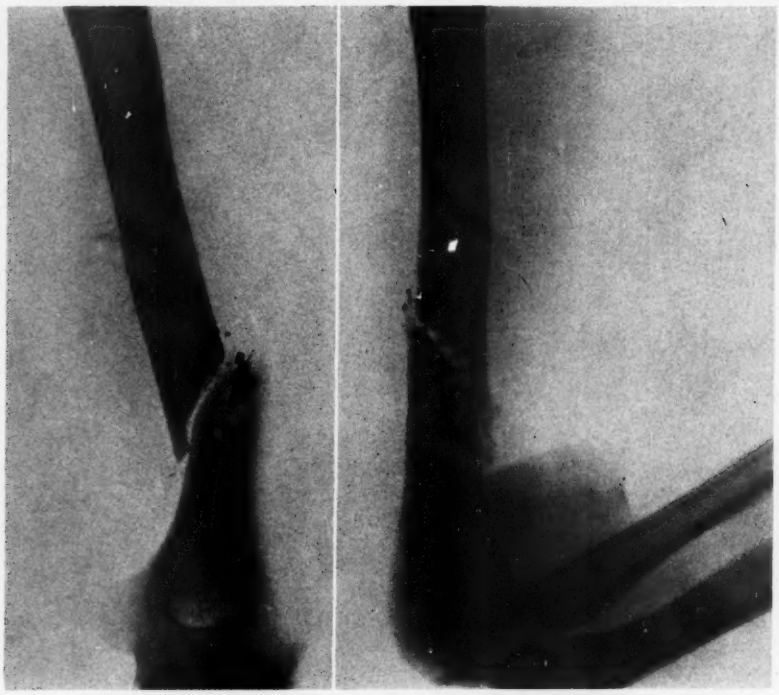
A B

FIG. 7. A, typical fracture of the midshaft immediately after application of cast. *X*-ray taken in supine position, so that fracture is not in position. B, the same fracture healed in good position with large callus.

A B

FIG. 8. Lateral views of same case as in Figure 7.

(Fig. 2A and B.) Fractures below the deltoid have no typical displacement except in the distal portion of the shaft, where a varus deformity may exist as in supracondylar fractures.



A B

FIG. 9. A, gunshot fracture of lower third of shaft showing typical varus deformity. Treated in full pronation in traction cast. B, the same fracture fifty-four days later. Good position and normal degree of healing.

Local anesthesia is used for fractures of the shaft, and gross reduction is obtained by manual traction and manipulation. The traction cast completes reduction just as suspension-traction methods reduce fracture of the shaft of the femur. Under the influence of traction the taut fibromuscular structures about the bone squeeze the fragments into place. The cast should not weigh over 3 pounds, especially in transverse fractures, which may be easily distracted by a heavy cast. In many transverse fractures it is sufficient to apply a "sugar tong" coaptation splint of plaster, extending from the axilla, around the elbow and up to the insertion of the deltoid. The wrist is suspended by a sling. The unsupported portion of the arm and forearm supplies sufficient traction force.

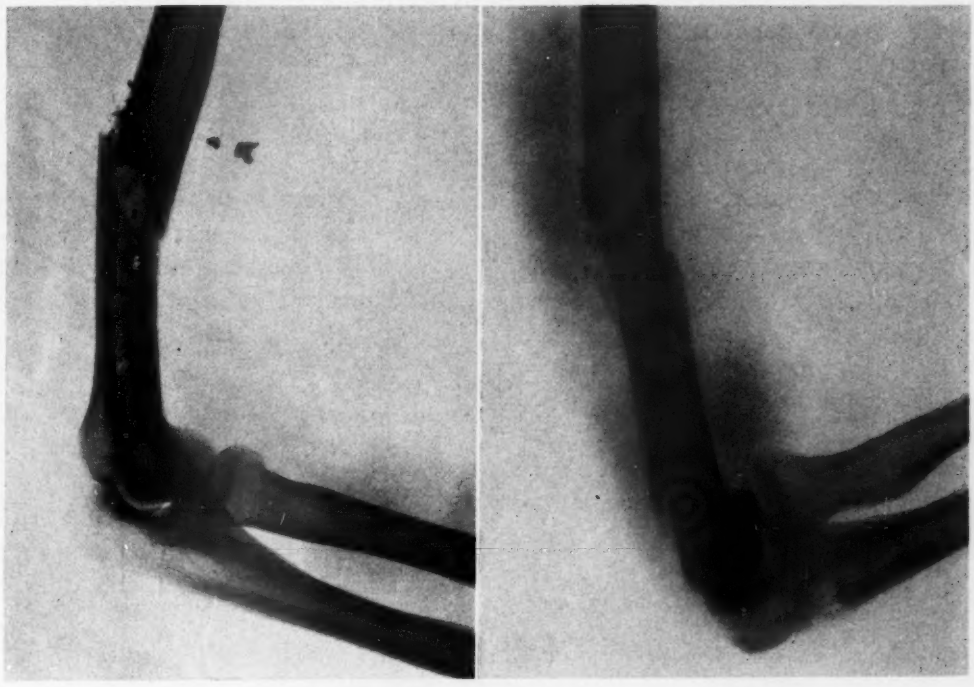
Varus deformity occurs in fractures low in the shaft and in the supracondylar region. Because of the break in continuity of the humerus the strong supinating action of the biceps is lost. The elbow joint comes under complete control of the strong pronators and is held in full pronation. Attempts to place the forearm in even slight supination result in supination (varus deformity) at the fracture site, since the joint is fixed by the pronators. (Fig. 3A and B.) Supracondylar and low shaft fractures are therefore placed in full pronation during and after reduction and the cast is applied in this position.

"T" and "Y" fractures of the condyles are reduced by traction with the elbow at a right angle and the forearm pronated. At the same time bilateral pressure is applied to push the condyles together. The cast is applied in full pronation to prevent varus. The same procedure and position are used in isolated fracture of the medial condyle. Fracture of the lateral condyle, which is likely to be followed by

valgus, is fixed in full supination to prevent this deformity.

The Traction Cast. (Fig. 4.) After anesthesia and reduction, a padded or non-padded plaster cast is applied from the knuckles to the axilla without regard to the site of fracture. The forearm is placed in mid-pronation unless full pronation or full supination are required, as shown above. The elbow must be at an exact right angle, so that with the patient erect and the forearm horizontal the distal fragment is vertical. A loop of wire or plaster is incorporated in the upper side of the cast at the wrist. A sling from this loop about the neck completes the dressing. The sling is placed through the loop rather than about the wrist to prevent sliding. The more distally the sling is placed the greater the traction applied to the arm and vice versa.

After-Care. The patient is instructed to remain erect as much as possible and for the first few nights should sleep in Fowlers's position. After the first week there is little possibility of displacement at night if the erect position is maintained during the day. At first the patient must be cautioned against resting the elbow on the arm of the chair when sitting. He soon learns, however, that he is more comfortable with the elbow unsupported, so that the traction fixes the fracture. Pressure from clothing, as from a buttoned coat over the cast, must be avoided. Anything that compresses the arm against the body interferes with traction.



A B

Fig. 10. Lateral views of same fracture as in Figure 9.

Circumduction exercises for the shoulder are taught and encouraged from the start. The patient leans forward and toward the injured side as far as possible, letting the arm hang free in a vertical position, the wrist still supported by the sling, and the muscles relaxed. He then swings the arm in increasingly larger circles embracing all motions of the shoulder to the limit of tolerance. (Fig. 5.) If properly carried out, this excerise will hasten convalescence and largely prevent restriction of shoulder motion. Even in fracture of the head and neck of the humerus, there is little or no atrophy of muscle.

In fractures of the shaft, care must be taken throughout the period of healing

to see that the sling is of proper length. The most common error is the use of an overly long sling. This allows the wrist to drop below the horizontal plane and swings the distal fragment of the humerus forward. Anterior bowing of the fracture then occurs. Conversely, a sling too short may cause posterior bowing.

This traction cast has been used by us in 128 consecutive cases of fracture of the humerus. Of these forty-nine were in the head and neck, sixty-eight in the shaft and eleven supracondylar and condylar. The fractures in the two extremities of the bone all healed with joint function superior to our previous results with any other methods. Of the fractures of the shaft all healed in good position with good function, with one exception. This patient was the brother of a physician. Open operation was carried out two weeks after fracture to remove interposed soft tissue. No internal fixation was used. Nonunion resulted, probably from reëngagement of muscle between the fragments.

SUMMARY

1. A simple effective method for treating fractures of the humerus is presented.

2. The method depends upon traction in the position of neutral muscle equilibrium.

3. It is applicable to almost all cases of fracture of the humerus.

REFERENCES

1. Caldwell, John A. *Ann. Surg.*, 97: 161–176 (Feb.) 1933.
2. Howard, Nelson J., and Eloesser, Leo. *J. Bone & Joint Surg.*, 16: 1–29 (Jan.) 1934.
3. Cotton, F. J., and Morrison, G. M. *New England J. Med.*, 211: 924–925 (Nov. 15) 1934.
4. Anderson, H. M. *Brit. M. J.*, 1: 232, 1934.

FACTS AND FALLACIES IN THE TREATMENT OF RECTAL CANCER

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CANCER has absorbed the attention of man from time immemorial. It has been attacked with weapons ranging from witchcraft to surgery. Great philosophers, theologists, scientists, and clinicians have devoted untold time to pondering upon it. From this vast amount of energy have sprung innumerable nostrums and a few facts.

Let us, then, forget if we can, the vast suffering which has followed the publication and practice of these various nostrums and consider how best to utilize our facts.

MARTIALLING OF FACTS

Nature of Cancer. Cancer is a change within the cell itself. It is presumably a disturbance of the intracellular chemical balance. It causes the cell to grow and multiply without consideration for its function nor for its anatomic boundaries. It enables the cell to flourish on less oxygen than is needed to preserve the viability of normal cells. It withstands transplanting readily.

Origin of Cancer. Two factors are known to be necessary to the production of experimental cancer. First, there must be an outside irritative factor. This may be physical or chemical. It must be applied over an appreciable portion of the life span of the animal. Synthesis of estrin has given researchers a quantitative and qualitative irritative agent which should greatly facilitate their labors.

The second necessary factor is an inherent susceptibility to cancer. This has been demonstrated through the inbreeding of mice by which means cancer and non-cancer strains have been developed very much in accordance with the Mendelian theory. Further, it has been possible to produce strains having not only a cancer diathesis but a marked propensity to develop cancer of certain sites.

Thus, the experimenter may apply a known quantity of an irritative agent for a known time to an animal of known cancer propensity and prophesy accurately the time and place at which a cancer will appear. This, naturally, leads to speculation as to viruses, toxins, antibodies, and immune bodies.

Growth of Cancer. Cancer grows without regard for physiology or anatomy. It spreads by continuous invasion of surrounding structures and by metastasis. Experimentally, it has been shown that growth will continue after the outside irritative factor has been discontinued unless the degree of susceptibility is extremely small. In these latter cases spontaneous retrogression and even total disappearance may be observed.

Metastasis. Cancer spreads through the vessels of the lymphatic and the blood systems. Those cells which find their way into the lymph channels are arrested at each node and can only proceed further after the gland has been severely damaged. Cancer emboli in the blood stream proceed swiftly on their course until trapped in a vessel whose lumen is too small to afford them passage. Hence, emboli from the alimentary canal are almost certain to be lodged at the portosystemic junction in the liver. Also, it is obvious that liver metastases will be more common than systemic ones from primary tumors of the digestive tract since the latter are mainly derived from cancer cells which pass via the lymphatics through the receptaculum chyli into the left innominate vein. Presumably, some metastatic emboli are thrown directly into local arteries but the results of these accidents are negligible.

UTILIZATION OF FACTS

Through study of these facts, three main forms of therapy emerge.

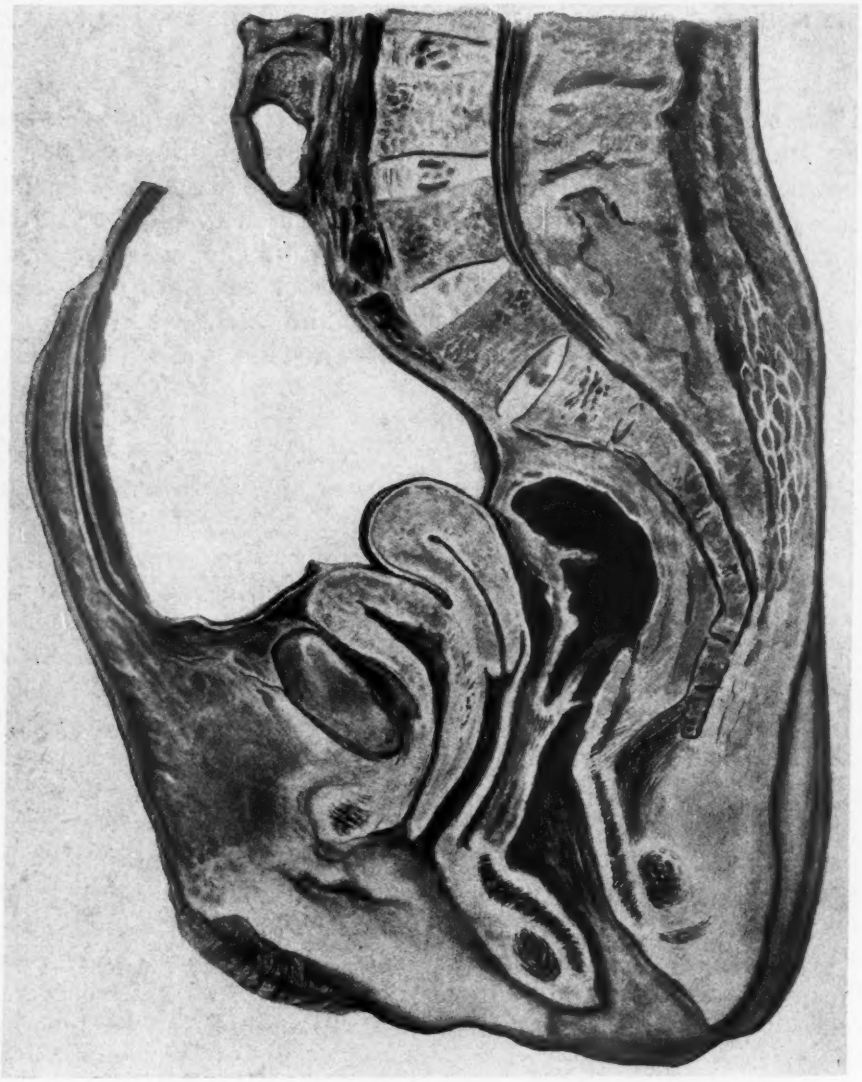

FIG. 1. Sagittal section through a child aged 14 years. Note rectal sheath and the manner in which the attachments of the levatores ani and superficialis sphincter ani facilitate its separation from the hollow of the sacrum. (From Lynch's "Diseases of the Colon and Rectum.")

First, one may attempt to produce some form of active or passive immunity. To date, no such weapon has been devised. Therefore we, as practical clinicians, must abandon this field to laboratory workers.

Second, one may attempt to destroy the cancer cell by radiation. This method depends for its success upon the fact that cancer cells are more readily destroyed by radiation than are normal cells. Unfortunately cancer of the digestive tract, and especially of its caudad end, is radioresistant and its metastases are even more so. In addition, radiation of lymphatic and systemic metastases tends to produce painful sloughs, while the liver metastases cannot even be attacked. Further, the margin of safety between the dose that will destroy cancer but not normal cells is so small that horrible catastrophes occur. Radiation has been known not only to stimulate the rate of growth of a cancer but even to serve as the necessary irritant

to convert a normal cell into a malignant one.

Many "cures" are merely the arrest of immediate growth and lymphatic spread by the formation of a barrier of fibrous tissue. This of course does not prohibit metastatic emboli since these may occur so long as a single malignant cell may enter a blood vessel. Late results of this formation of fibrous tissue are the production of persistent pain and damage to adjacent organs through its contraction. These symptoms may not present themselves until years after the patient has been pronounced "cured" and treatment discontinued.

True cures of rectal cancer by radiations do occur. These are cases in which the patient's susceptibility was extremely low.

In view of these facts, we must regretfully restore this field of endeavor to the experimentalists.

Third, one may attempt to cure the condition by surgery. To this end, let us define the desiderata. They are to remove surgically all cancer cells and completely to rehabilitate the patient. Obviously, the easiest time to do this is when the growth is small and metastases have not yet occurred. Thousands of men have wasted millions of words in attempting to provide surgeons with cases of early cancer. Most cases are not diagnosed until nine to thirteen months after the inception of the growth. This is not due to the difficulty of making a diagnosis but to the absence of the opportunity for an expert to make an examination. An obvious cure is to insist upon a routine sigmoidoscopic examination biannually. This will demonstate neoplasms at a time when local removal will ensure a cure.

CHOICE OF OPERATION

However, it is the late cases of cancer about the rectosigmoid with which this paper is concerned. As to the earliest lesion which demands more than local excision, the surgeon's own good judgment must suffice. The opposite end of the scale is reached only when carcinomatosis is present or when the patient's general condition cannot be sufficiently improved to offer any hope of surviving the operation. This statement is based on three facts. First, that the operability of a case can only be determined at operation. Second, removal of the primary growth obviates an imminent and painful death and at the worst converts it into a "liver death" which is distant, swift, and comparatively painless. Third, that the removal of the primary growth, in part or in toto, may permit disappearance of both primary and secondary lesions in persons of slight susceptibility to cancer.

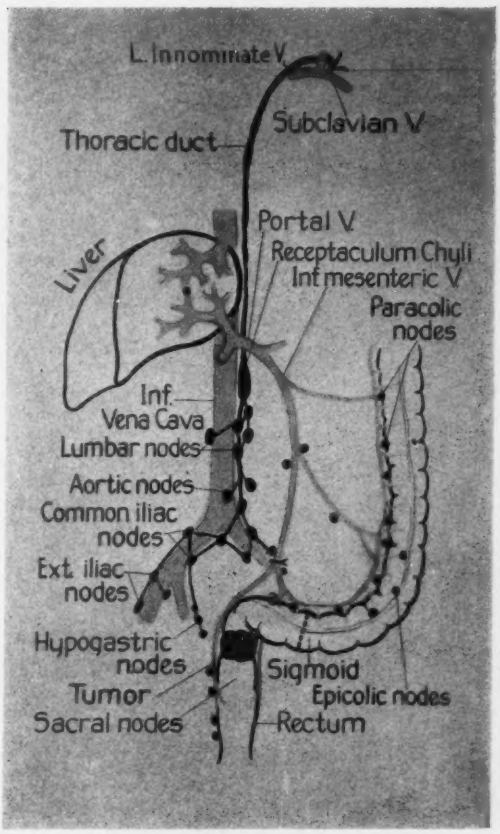

Fig. 2. Chart showing: (1) lymphatic drainage of rectum and sigmoid; (2) absence of afferent lymphatics to liver; (3) cancer cell trapped at portosystemic junction in liver; (4) dotted line indicates safe point of excision for a cancer as shown; and (5) this is the area included in our modified perineal technique.

As we have seen above, metastases are microscopic emboli which are projected

either into the blood stream or into the lymphatic circulation. Once they have entered the portal circulation they are beyond the reach of any surgery. They will become trapped within the venous network of the liver and either perish or grow at about the same rate as the primary lesion. Hence we cannot diagnose the presence of metastases in the liver until many months after their occurrence when they have grown sufficiently to constitute a palpable tumor. We may, however, suspect their presence when ulceration of the primary growth is found.

For these reasons, palpation of the liver is a useless procedure and should not be allowed to affect the choice of operative technique.

Since the lymphatics are invaded in the same manner, palpation of indurated nodes can give little real information. This is true even after metastatic invasion is pronounced since even experts frequently mistake inflammatory glands for carcinomatous ones. Cuthbert Dukes[1] found a 61 per cent error in the clinical diagnosis of carcinomatous glands.

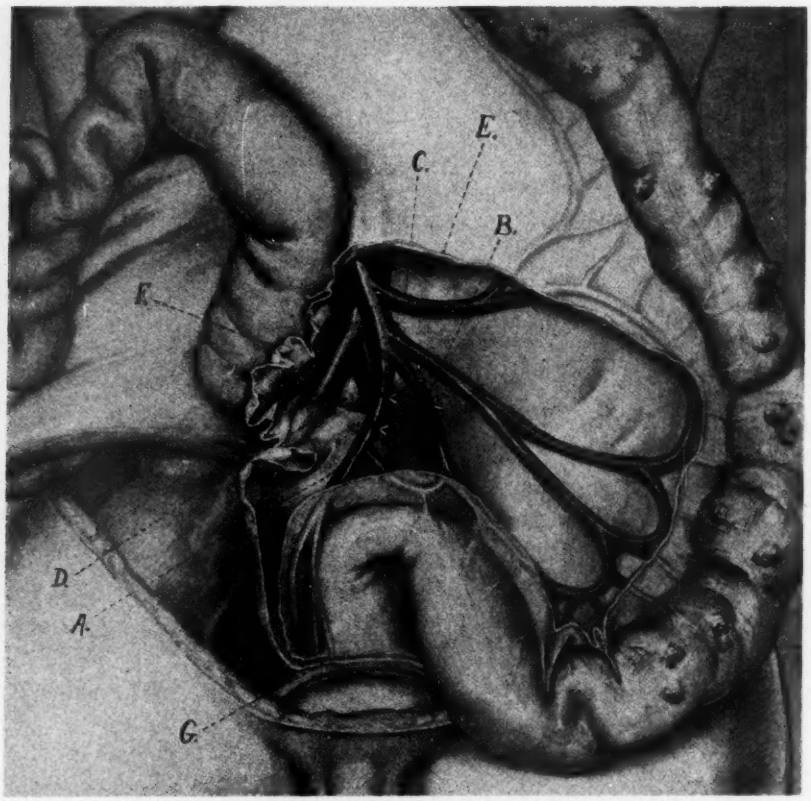

FIG. 3. Shows similarity of the areas removed by the combined and by our own simplified technique. (From Lynch and Felsen, "Tumors of the Colon and Rectum.")

However, since the course of the lymphatics draining a given area is known, an operation may be planned for excision of all those customarily affected. To this end, let us describe the lymphatic drainage of the anus, rectum and rectosigmoid briefly. The anus and lower part of the rectum drain mainly into the inguinal glands, superficial and deep, and thence through the external and common iliac nodes to the main abdominal trunk. A few channels connect with those accompanying the superior hemorrhoidal vessels.

The ampulla and rectosigmoid drain mainly into the lymphatics coursing with the superior hemorrhoidal vessels to the mesenteric nodes and thence through

subaortic and aortic groups to the cysternum chyli. The middle hemorrhoidal gland also drains this area directly into the common iliac nodes. The sacral glands receive lymph from the rectum which they pass through the hypogastric to the aortic groups of nodes. Those on the sigmoidal side drain through the epicolic and paracolic nodes to reach the inferior mesenteric group and thence through the aortic groups to the receptaculum chyli.

Metastases invade each node of a chain in turn. Very rarely, an aberrant vessel may give the impression that the invasion has skipped a gland.

Retrograde and lateral spread can occur only when a collateral lymphatic circulation has been established after complete obstruction of the normal channels.

It has been found that in cancer of the rectum few cases come to operation in which the inferior mesenteric nodes are involved. Cuthbert Dukes sectioned over 2,000 glands from 100 cases of cancer of the rectum removed by the perineo-abdominal technique. He found the paracolic nodes to be invaded in only one case and that was an extremely late one in which retrograde and lateral spread had already occurred. "Skipping" also was present in one case.

Glandular involvement was present in sixty-two cases, of whom thirteen had only one gland involved, eleven, two, seven had three, and thirty had four or more glands involved.

The average distance of the cephalad involved gland from the anal margin was 21.25 cm. in twenty-four cases of Gabriel's from the above series. The superior hemorrhoidal vessels were ligated 25.4 cm. from the anal verge.

Hence it is reasonable to suppose that any operation which will remove an average of 25.4 cm. of caudad bowel together with its portion of the superior hemorrhoidal chain should give an excellent prognosis. If the operator removes the middle hemorrhoidal and sacral nodes as well the outlook becomes even brighter.

The abdominoperineal operation of Miles fulfills the first of these requirements but the second is difficult to achieve. This is because the sacral nodes lie in a plane difficult of access from the abdomen.[2] In addition, the operation is attended by a very high mortality even in the hands of experts.

The perineo-abdominal operation is a far better one. First, because the long stage of the operation is almost devoid of shock. Second because the approach facilitates the removal of the sacral and middle hemorhoidal nodes with the specimen. Third, because quite frequently the operator is agreeably surprised to find that the objective has been attained without the necessity of opening the abdomen.

This operation also has a high mortality and therefore should give way to a perineal excision of the rectum so modified as to attain the above desiderata with little danger of death. This operation has already been described.[3]

The important modifications are:

1. The incision between the tuberosities of the ischii is curved anteriorly. This allows an easier definition of the line of cleavage between rectum and anterior structures.

2. The coccyx is removed by incising its joint and rotating it backward and downward. This permits ligation of the middle sacral artery before it is damaged and before it can retract into the soft tissues. Also the attachments of the superficialis sphincter ani and the levatores ani to the cocyx and sacrum almost force one to remove the rectal sheath with the specimen and with it the sacral nodes. If, on the other hand, the coccyx is left in situ or these muscles are cut before its removal, the line of cleavage and the sacral nodes may be difficult to define. The removal of the coccyx also provides free drainage of the wound and permits the formation of a better functioning perineal colostomy.

3. The puborectalis is used as a guide to separate the rectum from anterior structures.

4. The bowel is freed and brought down with a safe blood supply by clamping and cutting the individual vessels close to its wall. Then a ligature is placed about the pedicle of the superior hemorrhoidal vessels, and the vessels, nodes and connective tissue distal to it are removed in one piece.

5. It is sufficient to retroperitonealize the stoma and it is not necessary to bring the gut to the skin edge. The bowel eventually will find its way down to meet the skin edge. This allows the removal of that portion of the bowel which extends from the new peritoneal floor to the skin. In most cases as much bowel can be removed as with the combined technique.

6. The wound is left wide open and heals by granulation.

7. The wound is packed with gauze soaked in 10 per cent tannic acid in alcohol. This produces an albuminate strong enough to prevent saprophytic infection but not strong enough to permit virulent organisms to grow under cover of it.

8. These two procedures obviate the risk of sepsis and hence of secondary hemorrhage.

CONCLUSIONS

1. Surgery offers the only possible cure for cancer of the lower bowel today.

2. Liver metastases cannot be palpated even at laparotomy until the organ is grossly involved.

3. No lymphatics run to the liver.

4. Lymphatic spread can be predicted.

5. Abdominoperineal and perineo-abdominal operations remove no more growth nor metastases in cancer of rectum than can be removed by our technique.

6. The so-called radical operations deserve the name because of their high mortality and not because they afford a more complete excision of the growth.

REFERENCES

1. Gabriel, W. B., Dukes, C., and Bussey, H. J. R. Lymphatic spread in cancer of rectum. *Brit. J. Surg.*, 23: 395–413 (Oct.) 1935.
2. Todd, T. W. Anatomy of a case of carcinoma recti. *Ann. Surg.*, Vol. 58.
3. Lynch, J., and Hamilton, G. J. Lynch's simplification of perineal excision of rectum. *Am. J. Surg.*, 36: 618, 1937.

THE PREVENTION OF PAIN FOLLOWING HEMORRHOIDECTOMY*

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THROUGHOUT the years rectal surgery has enjoyed an unenviable reputation for postoperative pain and discomfort. This fear has not been entirely unfounded in the minds of laymen and physicians. To advise a rectal operation, or even a rectal examination, all too frequently brings forth a gasp of horror from the patient. Nearly every individual with a rectal disorder seems to know some one who was operated upon and endured torturing pain. The picture is not overdrawn, but the situation is no longer justifiable. This is a timely problem which presents itself to every proctologist and surgeon. The crusade for the early diagnosis and the early treatment of irritative rectal lesions is definitely obstructed by this widespread notion.

Innumerable patients have put themselves into the hands of "pile doctors" and so-called rectal sanitariums in their search for alleviation the "easy way." Many more delay treatment until their condition has become advanced or complicated.

To secure for the patient about to undergo a hemorrhoidectomy, not merely a modicum of postoperative comfort, but a painless or nearly painless convalescent period, should be the aim of every surgeon undertaking a rectal operation. This goal has been and can nearly always be achieved, provided the surgeon is ever mindful of the following elemental rules which should govern any type of surgery:

1. Close attention to certain basic surgical principles. To quote Sumner Koch:[1] "Nihil nocere—do no harm. What does 'do no harm' mean? It means, first, to avoid every form of injury, mechanical, thermal, chemical; and secondarily, not to add contamination to that which is already present. Third, to avoid so far as possible, leaving foreign bodies in the operative wound."

2. The application of that expert and particular care to which this area, as one of the most sensitive regions in the human body, is entitled.

3. The utilization of a tried and tested routine preoperative and postoperative régime.

4. The selection of an open, non-burning, non-traumatizing type of operation.

Following these tenets, I have found that post-operative pain has become the exception rather than the rule.

The skin at the anal orifice is one of the most sensitive areas in the whole body, sharing this distinction with the mouth, lips, fingers, and toes. There are two senses: one is tactile, produced by contact with the mucous membrane of the anal canal; the other is the muscle sense, which may be described as the sensation caused by the stretching action of the muscle due to something within its grip. The sensitive area is practically confined to the anal canal proper. Hemorrhoidectomy, of necessity, implies interference with this sensitive area. Almost all the sensations at the anal orifice have for their immediate object, some alteration in the state and degree of contraction of the sphincter muscle, the action of which is almost entirely reflex in character. It is, therefore, easy to understand why operations in this area are liable to result in pain, since the wounds

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cause constant irritation of this reflex with consequent spasm and painful contraction of the muscle.[5]

There are surgeons who believe that they have found the answer to this problem by the use of slow absorbing, oily anesthetics. I will not say these drugs are inadequate in all cases, but it is my feeling that they are superfluous. The complications from their injudicious, and sometimes from their judicious use have not been sufficiently emphasized or even reported. To depend upon the action of a drug for an end which can be and should be achieved by exact, clean workmanship is unsurgical and unphysiologic. Since the introduction of benacol in 1927, by Yeomans[2] and his co-workers, there have been at least six or seven variations to this formula launched upon the medical market. Time and experience will relegate these foreign body substances to the rôle for which they were originally intended: for minor simple fissures and perhaps as an adjunct to the treatment of pruritus ani. I have noted that in comparing patient for patient, the healing process is retarded in the presence of these oily substances.

The steps necessary to achieve the goal of a painless or nearly painless hemorrhoidectomy convalescence must be divided into three stages: preoperative, operative and postoperative.

Twenty-four hours prior to hospitalization (unless there is some contraindication) a 6 ounce dose of citrate of magnesia will start elimination well on its way, and offset postoperative gas pains, which are so troublesome to patient and physician.

The patient should enter the hospital on the evening before the operation. A plain water enema is administered, followed by the instillation of 4 ounces of olive oil as a retention enema. This is expelled in the morning and the rectum is further cleaned with a plain water enema. All unexpelled water must be syphoned away. These procedures will usually relieve the patient of any desire to eliminate for at least three days after the operation. The use of castor oil and other aperients on the night before the operation will cause postoperative discomfort and leakage on the operating table.

A restful sleep the night before the operation is of more importance than any other factor in reducing pre-anesthetic fears and psychic trauma. Important, too, is the rigorous insistence that the patient shall not be roused at 4 A.M. to be prepared for an 11 o'clock operation.

The use of a basic anesthetic is a matter of choice, in which the individuality of the patient must be a determining factor. In most cases 3 to 6 gr. of sodium amytal the evening before, and 3 gr. again the first thing in the morning, followed by dilaudid gr. $\frac{1}{20}$ one hour before the operation, will bring the patient to the operating room in a sufficiently relaxed condition and oblivious to the operating room activities.

A point which may seem to be minor, but is assuredly of great importance to the patient is the perianal shave. Some operators have eliminated this procedure from the routine, feeling that the subsequent bristle discomfort does not warrant its use. I still order the perianal shave. This, too, can be carried out carefully and cleanly without cutting, scratching, or tearing. It is sometimes difficult to rid this area of small hairs in the presence of large folds and skin tabs, but an experienced orderly can make this step at least endurable.

There is no justification for applying tincture of iodine or any other alcoholic antiseptic solution to a freshly shaved perineum, especially where mucous membrane may, at times, be prolapsed and exposed. Vigorous soap and water cleansing, followed by an aqueous antiseptic, such as 5 per cent mercurochrome, has proved very effective.

A factor of major importance in reducing the postoperative discomfort is the choice of anesthetic. The success of the operation depends greatly on the knowledge of the possibilities of the anesthetic procedure

employed. Certainly no general anesthetic need be employed for hemorrhoidectomy. The only possible exception to this rule might be in the presence of gangrenous strangulation. Regional anesthesia possesses decided advantage over general narcosis. The absence of postoperative vomiting, retching, coughing, and straining which are instrumental in the formation of perianal edema, skin tabs, and pain (due to strain and pulling of sphincter), and the absence of acute distention of the colon, argue for the use of regional anesthesia.

The practice of regional anesthesia is an art. It requires special knowledge of anatomy; skill in the performance of its various procedures; experience in the handling of the patient; and above all, gentleness in execution of surgical procedures.[3] The type of regional anesthetic will depend upon the patient, the experience of the surgeon, and the pathology at hand. Low spinal, local infiltration of novocaine, and caudal or sacral anesthesia, all have proponents and are all used more or less successfully.

Novocaine infiltration anesthesia will be found to fit very easily into the list of methods offering a minimum of postoperative discomfort. A thorough knowledge of perianal innervation and of the anal and perianal anatomy is required, but no more so than is required to perform skilful rectal surgery. Fifty to 80 c.c. of a one-half or 1 per cent solution, plus approximately 5 to 8 drops of adrenalin to the ounce is sufficient for successful anesthesia and sphincter relaxation. Care must be taken not to produce subcutaneous distortion, especially in the presence of external tabs, as this may lead to the injudicious removal of excess perianal skin and subsequent contraction and pain. Novocaine infiltration anesthesia can be used with any type of operative technique. If the novocaine is properly placed, the sphincter will relax almost immediately.

Operations for internal or external hemorrhoids have, for many years, been performed by means of local infiltration around the anus irrespective of the operative technique adapted. Dilatation of the sphincter, in addition to the anesthesia, is nearly always successful. The relaxation of the sphincter immediately follows the proper injection of the anesthetic solution, thus eliminating the necessity for manual or instrumental dilatation. The practice of inserting the finger into the anus so as to prevent the point of the needle from entering the anal canal and rectum, is not without risk of contaminating the healthy surrounding tissues. The finger should be inserted by all means, but a change of gloves should be made. Low spinal anesthesia, using 25 to 50 mg. of procaine hydrochloride, will afford saddle anesthesia and good sphincter relaxation. This type of regional anesthesia has been popular with the English school of proctologists. Many surgeons have questioned the feasibility of spinal anesthesia where local infiltration offers such a good substitute. The work of Davis[4] demonstrating the adverse action of spinal anesthetics on the myelin of the nerve fibers, has deterred an increasingly large number of operators from its routine use.

Sacral block anesthesia has its proponents. This is produced by subdural injection low in the spinal column. The anesthetic is used in a small dosage and is well concentrated so that the area of anesthesia remains low. Those favoring this method of regional anesthesia like its limitation to the field and the ample sphincter relaxation without distortion.

Caudal block gives almost the same results as far as operating advantages are concerned, that is, perfect anesthesia with partial sphincter relaxation. It has a marked advantage over local infiltration in that the injection is made at a distance from the operative field. The occasional failures to produce anesthesia by means of caudal block alone and the slowness with which the anesthesia sets in suggest its possible use in association with transsacral block.

A major factor in producing severe postoperative pain is the vicious and strictly uncalled for procedure of divulsing the sphincter muscle. This maneuver is by no means a thing of the past. It is carried out daily in many operating rooms. The attempt to prevent postoperative pain by stretching the sphincter ani with the idea of causing temporary paralysis, is based on a false premise. It is not successful because, unless the muscle is actually damaged, the paralysis is too transient, not lasting more than thirty minutes in most cases and often not that long. The reason for this is that the muscle, in the process of recovering its powers of contraction, will contract spasmodically, causing sudden violent pain each time the spasm occurs. One must think of the intramuscular bleeding that occurs when the sphincter muscle fibers are torn. I say torn, because no matter how gently this muscle is dilated, some of the annular fibers at least are bound to give way. I have witnessed the insertion of one finger after another into the anal canal until nearly the entire hand passed through the orifice. This procedure, while not as frequent with local anesthesia, is still carried out routinely by a surprisingly large number of operators.

Even when the thumb and forefinger are inserted, a great deal of spasm results because of the unmeasured and unrealized force used. All theories upholding sphincter divulsion are purely hypothetical. The fact remains that patients operated on without preliminary divulsion are many times happier and more comfortable than are those in whom divulsion is carried out. The mechanical divulsor which, strangely enough, is seen in many operating rooms of modern hospitals has been the cause of partial incontinence.

It would be difficult to find two surgeons performing a hermorrhoidectomy in the same manner. Indeed, one would not expect nor desire to see such standardization of surgical technique. Nevertheless, it is apparent that some methods of hemorrhoidectomy lead to more postoperative pain than do others. The operative procedure which will remove the fundamental pathology with the least amount of trauma logically becomes the operation of choice. With this in mind, I have found the ligature transfixion operation as practiced for years at St. Mark's Hospital in London to fulfill the requirements. I do not believe that any technique which involves the use of the cautery, the wide dissection of perianal tissues, or the placing of multiple sutures, as coming within the category of a choice operation.

It is well worth remembering that even in a choice type of operation, there are certain errors of omission or commission which spell the difference between pain and ease to the convalescing patient, as the following points will indicate:

1. The ligature which is passed around the varicosity should be pulled snugly enough to produce hemostasis, but to pull this ligature with all one's strength will cause more postoperative pain.

2. Chromic catgut, silk, kangaroo tendon, or linen causes more pain than plain No. 0 or No. 1 catgut.

3. The mucous membrane covering the pile must never be stripped high so as to leave a large denuded area. If stripped above the level of the anus, painful contracture will result.

4. The forceps used to grasp the hemorrhoids should be of a type which will not tear the delicate tissues. The Allis forceps fulfil this requirement very well. Only gentle traction need be applied.

5. In placing the ligature around the hemorrhoids, great care should be exercised so as not to include muscle in the bite. If this is done it will cause painful contractions of the sphincter ani during convalescence.

6. External hemorrhoids and redundant skin must not be removed in excess. Fine judgment must be exercised or large gaping wounds will cause no end of pain and burning.

7. The removal of an insufficient amount of redundant skin with correction at a later date is far better than the

removal of an excess at the time of the operation.

8. Remove external hemorrhoids, leaving a triangular wound with the base pointing laterally; this will afford sufficient drainage and smooth healing.

9. Islands of skin should be left between areas removed to avoid painful contraction.

10. Care must be taken not to cut too deep. Muscle excised cannot be replaced. Bleeding points should be controlled by temporary pressure with gauze or forceps.

11. Suturing of the perianal skin causes pain, infection, and reduces drainage.

In completing the operation, it is customary for many surgeons to insert a plug, tube or drain into the anal canal. This procedure is second only to divulsion as a cause of postoperative discomfort. The sphincter will contract down on the foreign body rhythmically in an attempt to expel it from its grasp. Each contraction is more painful than its predecessor. The injection of a tube of vaseline, liquid or solid, or some soothing anesthetic ointment is all that is needed.

A dressing should be applied in the operating room which will fit snugly and not slip as soon as the patient is put to bed. To readjust a dressing within an hour or two after operation is productive of pain.

With the patient back in bed, a systematic postoperative régime should be started. The dressings should not be disturbed for a few hours unless there is good reason for such an action. An electric pad (rubber covered) may be adjusted to the buttocks; aspirin compound may be given in moderate doses every two or three hours. Within five or six hours, the bandages are carefully removed and hot wet packs are applied and kept hot by frequent changes. A wad of cotton soaked in witch hazel placed next to the anus is soothing, antiseptic and astringent.

The patient is kept in bed for the first two days. On the third day the administration of hot sitz-baths, two or three times daily or as often as the patient desires, is begun. The wound is irrigated daily with an asepto syringe and a witch hazel and water solution. No attempt is made to start elimination until the evening of the third postoperative day when a warm olive oil retention enema is given with small catheter and bulb syringe.

Traditionally, the first bowel movement is painful. This is not necessary if a few precautionary methods are taken immediately before and after the bowel movement. A hot sitz-bath after elimination will add to the patient's comfort. The anus should be irrigated after each bowel movement. A dressing of liquid or solid vaseline or some soothing anesthetic ointment should be applied. There is no need to insert the finger into the anus until healing has well begun. After the seventh or eighth day, it is well to pass the gloved finger once or twice a week until healing is completed. The patient can apply vaseline or any soothing ointment daily by means of a finger cot.

A soft low residue diet is recommended for the week immediately following operation.

Hospitalization need not extend over five days in uncomplicated cases.

CONCLUSIONS

Traditional postoperative pain following a hemorrhoidectomy is avoidable and unjustifiable.

Comfortable convalescence can be achieved by: (1) avoiding all unnecessary injury to anal tissue; (2) the application of expert and particular care to this most sensitive region; (3) utilization of a tried and tested preoperative and postoperative routine; (4) selection of an open, non-burning, non-traumatizing type of operation.

Operations involving the use of the cautery, wide dissection of perianal tissues and the placing of multiple sutures lead to more pain than the simple ligature transfixion operation.

The practice of inserting plugs and tubes into the anal canal postoperatively as well as divulsing of the sphincter ranks high in the list of causes for pain.

Oily anesthetics are superfluous and are a poor substitute for cleancut surgery.

The traditional fear of the first bowel movement need no longer be a problem providing a few precautionary measures are taken.

REFERENCES

1. Koch, Sumner. Injuries of the hand. *J. A. M. A.*, 107: 1044–1048, 1936.
2. Yeomans, F. C., Gorsch, R. V., and Matheshеimer, J. L. Benacol in the treatment of pruritus ani (preliminary report). *Tr. Am. Proct. Soc.*, 28th annual session, pp. 24–32, 1927.
3. Labat, Gaston. Regional Anesthesia; Its Technic and Clinical Application. 2nd ed., Phila., 1928. Saunders.
4. Davis, Loyal, Haven, H., Givens, J. H., and Emmett, John. Effects of spinal anesthetics on the spinal cord and its membranes. *J. A. M. A.*, 97: 1781–1785, 1931.
5. Lockhart-Mummery, J. P., Diseases of the Rectum and Colon and Their Surgical Treatment. 2nd ed., Baltimore, 1934, William Wood.

The mechanism of injury [in fractures in the region of the hip] was generally a combination of direct and indirect violence from a fall. About 60 per cent were injured in their homes.

SELECTIVE SURGERY IN OPERABLE RECTAL CANCER*

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THE treatment of rectal cancer is an interesting but intricate problem. Extirpation of the rectum has been practiced since Lisfranc reported his successful operation in 1926, but during the past quarter of a century there has been a marked improvement in the surgical treatment of this disease. New types of operative procedures have been described, and the surgical technique of rectal resections has been greatly improved. Despite these improvements, there is not, as yet, any one procedure that is suitable for routine employment in all cases. Two factors, (1) the variation in the extent of disease at the time patients are referred for treatment, and (2) the variation in the ability of patients to withstand radical resection, make selective surgery preferable to the routine use of any one method.

The types of operation that have proven of greatest value and appear worthy of consideration in selecting treatment for operable diseases, are: (1) abdomino-perineal resections completed in one or two stages; and (2) perineal resections with or without preliminary colostomy. Each of the above procedures has a field of usefulness in the surgical treatment of this disease. Most appropriate selection can be made from the knowledge of the comparative advantages and limitations of each procedure, the pathologic factors of the disease presented, and the general physical condition and the psychology of the patient.

Early diagnosis is the greatest asset to successful treatment regardless of the method employed. Rectal cancer begins as a local disease in the mucosa and extends both by direct continuity of the disease and by dissemination through the lymphatic and blood streams. If it were possible, uniformly, to recognize cancer in the early incipient stages, treatment would be greatly simplified and excellent results obtained by the majority of the above methods of procedure. Unfortunately, many operable lesions are well established, often with involvment of the lymphatic and the adjacent tissues, at the time patients come under observation. As a rule, the extent of the disease has a marked bearing upon the prognosis, which, however, may be favorably influenced in certain instances, when the disease is no longer localized, by employment of more radical forms of surgery.

The ability of patients to withstand operation should be carefully considered. Certain types of resection are accompanied by greater degrees of shock and more severe complications than others. In most instances in the treatment of cancer in this location, it is advisable to employ the most radical dissection that the patient appears able to withstand, as one is never sure of the extent of the disease. The problem of selecting treatment is a comparatively simple one when dealing with patients in good physical condition. Unfortunately, rectal cancer frequently occurs in patients of mature and old age. Many of these patients are also victims of heart, lung, kidney, metabolic or other chronic diseases, factors which increase the hazards of successful resection. It is impossible to treat rectal cancer adequately without a certain percentage of operable fatalities. The latter, however, may be held at a reasonably low figure by attempting to keep the treatment within the tolerance of the patient and at the same time to afford him the benefit of the most radical resection that he is able to withstand. Operable mortality, in all types of resections, has been lessened by more careful preoperative

* Read before the American Proctologic Society, at Atlantic City, June 1937.

preparation, by liberal employment of blood transfusions, better surgery and more detailed after treatment.

By obtaining a careful history and by detailed physical and laboratory investigations, the surgeon may estimate the patient's ability to withstand operation to a rather accurate workable degree. In accordance with these investigations, patients with operable disease may be separated into four groups, (1) good, (2) medium, (3) poor, and (4) bad surgical risks. Although the primary disease may be removable in patients classified as bad risks, the poor physical condition contraindicates the employment of radical surgery.

Location of the tumor may also, at times, influence the selection of surgical treatment. The term, rectal cancer, frequently includes lesions situated anywhere from the anus to the rectosigmoidal junction. Low lesions, within reach of the index finger, may or may not be suitable for perineal extirpation, depending upon the extent of the disease and condition of the patient. The most appropriate approach for tumors in the upper rectum and at the rectosigmoidal junction is by way of the abdomino-perineal route, unless this form of surgery is contraindicated by the patient's poor physical condition.

Abdomino-perineal resection is the ideal surgical method of approach in eradicating rectal and rectosigmoidal cancers. This type of operation permits removal of the primary tumor with a wide dissection of adjacent tissues and lymph-drained areas. The terminal intestinal tract from the middle of the sigmoid to the anus is also removed. The patient retains a permanent colostomy. Abdomino-perineal operations may be completed at one time as advocated by Miles, or the dissection may be in two stages as suggested by Coffey, Rankin, Lahey and others. The choice between the one- and the two-stage procedures rests largely upon the general physical condition of the patient, the degree of obstruction, the degree of infection and the extent of the disease.

The one-stage or Miles' type of procedure has the advantage of being completed at one time. Patients are immediately relieved of the worries and fears of a second operation. Convalescence, if uncomplicated, is short, and the majority of patients leave the hospital within four weeks. The chief objection to the one-stage procedure, when it is routinely employed, is the accompanying high operative mortality. Miles, however, has shown that the mortality from his operation may be kept comparatively low by selecting suitable cases. Experience in the selection of cases and improvement in surgical technique tend to increase the popularity of the one-stage operation.

Two-stage abdomino-perineal resections have been devised to accomplish with a comparatively lower operable mortality a similar dissection to that afforded by the Miles operation. Of the two-stage procedures that have been described, the Lahey technique has received the greatest popularity. This operation appears to offer certain advantages over other two-stage procedures. The main objectionable features of this resection, outside of the inevitable two procedures, are (1) reopening the abdomen at the site of an intestinal stoma, and (2) contending with adhesions which, at times, follow the first procedure. Despite these objectionable features, operable mortality is quite low. Shock is seldom severe, and fatal peritonitis is relatively rare. The technique, as described by Lahey and his staff, has been followed in most of our cases. In a few instances, when dealing with large friable, borderline operable lesions at the rectosigmoidal junction, in order to lessen the likelihood of rupture into the bowel or tumor, we have modified the technique. The second operation is begun in the usual manner. After tying the superior hemorrhoidal artery and loosening the rectum posteriorly, the dissection is then completed from below and the tumor removed by the perineal route. The new pelvic floor is then constructed and the abdominal wound closed in the

usual manner. This technique converts the second stage into the abdominoperineal abdominal type of procedure. Whether this variation in technique is of any value under such circumstances will require additional experience to estimate fully.

Judging from a limited experience of fifty-six abdomino-perineal operations in which there was an operative mortality of 12.5 per cent, we think there is a definite field for both one- and two-stage procedures in the routine treatment of rectal cancer. One-stage operations appear to be best suited for good surgical risks with early or moderately advanced lesions. Two-stage procedures are suitable for medium surgical risks and for that small group of patients classified as good risks with badly infected, stenosing, borderline operable cancers. The percentage of clinical cures following these types of resections should be superior to that of restricted methods of surgery. Such results, however, will depend largely upon the extent of disease in those cases selected for this method of treatment.

When sufficient time has elapsed to compare the ultimate results of the one- and the two-stage abdomino-perineal operations, in all probability such results will vary more in accordance with the extent of disease at time of operation than with the method of procedure employed.

PERINEAL RESECTIONS

Perineal resections are limited operations in that there is less opportunity for dissecting the areas drained by the lymphatics than with the abdominal types of procedures. Limited dissections are capable of producing clinical cures only when all cancer cells can be removed. Perineal resections, therefore, from the standpoint of obtaining clinical cures, are best suited for cancers within the lower half of the rectum in which the disease is well localized. Such favorable conditions are encountered at times when the disease is recognized in the early stages and when the histologic report reveals a low grade of malignancy.

The extensive routine employment of perineal resection by many surgeons, as a method of eradicating rectal cancer, has been due to the low operative mortality following this type of operation, and to the high operative mortality which accompanied abdomino-perineal resections a decade or more ago. Operative mortality from the perineal operation in our clinic is less than 5 per cent. Because of this low mortality and despite its limited nature, this operation has a real field of usefulness in cases where patients in poor physical condition are quite unlikely to withstand more radical forms of surgery. The final results of perineal resections from most clinics are less gratifying than those following abdomino-perineal resections, although Lockhart-Mummery, in a recent communication, gives figures which compare favorably with the most radical procedures. The low percentage of clinical cures reported may be largely accounted for by the frequent employment of this type of resection in advanced stages of disease. It is often employed with borderline and inoperable disease and with patients in poor physical condition, the objective being palliation rather than clinical cure. Perineal resections are best reserved for that group of patients who, because of old age and chronic constitutional disease, are considered poor surgical risks, and for the small percentage of patients with low-lying tumors which still remain in the early stages of development.

The rectum may be resected by the perineal route, with or without the constuction of a preliminary abdominal colostomy. A preliminary operation permits exploration of the abdomen to determine the presence or absence of metastatic disease, and places the artificial anus in a convenient location for cleanliness and care. Preliminary colostomy often permits a wider dissection of the pelvis and the removal of larger sections of the rectum. The operative mortality is but little

influenced by a preliminary operation. Perineal resections without colostomy may be preferable when dealing with very obese patients and those who absolutely refuse to have an opening on the abdominal surface. Perineal stomas function satisfactorily in the majority of instances, but they are less accessible for irrigations and cleanliness than those situated upon the abdomen.

Operations that attempt continuity of bowel and sphincter control have not proved to be very satisfactory in the treatment of rectal cancer. Procedures such as local excisions, perineal resections with preservation of the anal sphincter, and abdominal resections with anastomoses have been employed in an effort to avoid a permanent artificial anus. We have had but little experience in performing the above types of resection, but have seen many recurrences in patients subjected to these operations from other institutions. The chief objectionable feature to operations devised to avoid colostomy is the high percentage of recurrences. Early recurrences are due to incomplete removal of the cancer. Resections with continuity of bowel and sphincter control have a limited field, and are best reserved for patients who absolutely refuse to be operated upon if they are to retain a permanent colostomy, and for a small percentage of early rectal and sigmoidal cancers that are favorably situated for limited surgical dissections. In many instances of early rectal cancer, eradication of the disease by radiation therapy which leaves the patient with a normal functioning intestinal tract, is preferable to limited surgical resections.

CONCLUSIONS

Selective surgery in operable rectal cancer is advisable because of variations in (1) the location of lesions, (2) the extent of disease, and (3) the physical condition of the patient. Abdomino-perineal resections, completed in one or two stages, afford the widest forms of dissection, and are preferable for the majority of patients who are classified as good and medium surgical risks. Perineal resections, with or without preliminary colostomy, are best suited for tumors situated in the lower two-thirds of the rectum in patients classified as poor surgical risks. Resections which attempt continuity of bowel and sphincter control have but a limited field in present day surgical treatment of rectal cancer.

THE CEREBRAL EPIDERMOIDS (CHOLESTEATOMAS)*

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INTRODUCTION

CHOLESTEATOMAS are a rare type of tumor encountered in various parts of the brain and cranium. Cushing found fourteen tumors of this type among 2,004 verified brain tumors. In the series of Dr. C. H. Frazier, eight cholesteatomas have been encountered at operation over a period of eight years. It can be seen therefore that their incidence is very low. Since these tumors are so strikingly different from other brain tumors in their histologic appearance, and since they are so readily removed surgically, it seems well to inquire further into their clinical features and into their methods of growth. For this reason I record eight cases of cholesteatoma from the collection of Drs. Francis C. Grant and C. H. Frazier. These were found in the following locations: cerebrum (parietal lobe), one; cerebellopontile angle, two; pineal recess, one; fourth ventricle, one; sphenoidal ridge one; suprasellar, one; occipital bone, one. The features of cholesteatomas in these various locations will be considered separately.

CEREBRAL CHOLESTEATOMAS

Cholesteatomas may be found in relation to any part of the cerebral hemisphere. They are not so numerous in the cerebrum as they are at the base of the brain or in the posterior fossa, but they occur with sufficient frequency over the cerebral hemispheres to warrant an analysis of their clinical features. They have been found in the frontal (Love and Kernohan[1]), temporal (Love and Kernohan, Nehrkorn,[2] Kakeshita[3]), parietal (Alpers, Critchley and Ferguson[4]), and occipital regions (Nehrkorn). (Fig. 1.) They are probably more commonly found in relation to the temporal lobes than to other parts of the cerebrum, and may lie within the brain substance or on it. When they lie within it, they represent tumors which have made a bed for themselves by compression from without, the brain enfolding them in this process. Sometimes they lie extradurally, compressing the brain from without. In such cases they may frequently be intradiploic cholesteatomas with extension into the cranial cavity and compression of the brain. Such cases show characteristic roentgenographic pictures due to destruction of the bone in the area of compression by the tumor.

Case 1 illustrates the clinical features of a cholesteatoma found in the left parietal lobe.

CASE 1. H. B. was admitted to the University Hospital on August 7, 1928, under the care of Dr. C. H. Frazier. She had had weakness of the right leg for fourteen years. This had remained unchanged until two years before entrance when she suddenly developed jerking of the right leg and foot followed by jerking of the right knee and finally of the abdominal muscles. These convulsive attacks were without loss of consciousness. Following them the weakness of the right leg became definitely greater so that she was unable to use this limb for a few days after an attack.

Examination revealed weakness of the right arm and leg, especially on flexion movements, increased tendon reflexes in the right leg, and a questionable Babinski sign. The rest of the neurologic examination was entirely negative. Ophthalmalogic examination revealed no papilledema.

An encephalogram, performed because of the few localizing signs, pointed to a lesion in the left frontal area. A large left frontoparietal

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craniotomy was performed by Dr. C. H. Frazier on October 25, 1928. A large tumor was found at the upper end of the left precentral and postcentral areas close to the longitudinal sinus. When this tumor was removed the cavity measured 10 cm. in length and extended down to the lateral ventricle. Grossly the tumor had the appearance of a cholesteatoma. Histologic study revealed a typical cholesteatoma with a characteristic capsule in which no keratohyaline was seen.

The patient made a good recovery and when last heard from in 1929 was well.

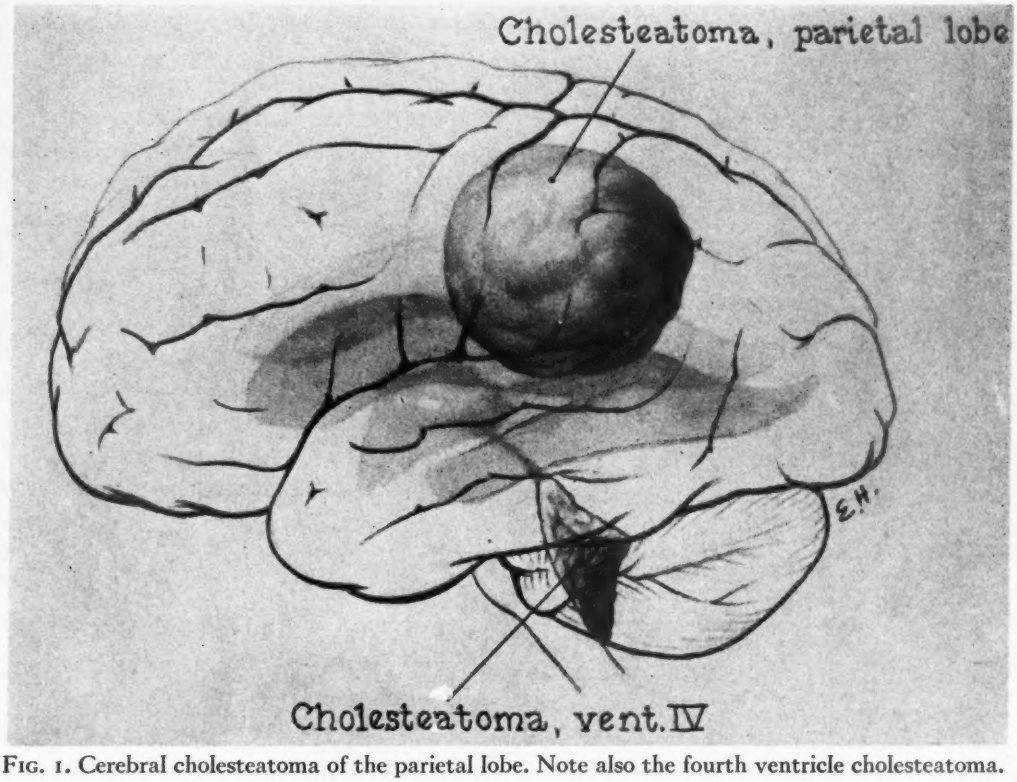

FIG. 1. Cerebral cholesteatoma of the parietal lobe. Note also the fourth ventricle cholesteatoma.

There is nothing in the clinical features of these tumors to differentiate them from other slowly growing brain tumors. They run a slow, progressive course, which, in the case recorded above, was of fourteen years' duration. It is only when cranial defects are seen in the roentgenogram that one is able to make a preoperative diagnosis clinically.

In Case 1 a good recovery followed the operation. Similar recoveries have been recorded by Learmonth and Kernohan[5] in a frontal lobe cholesteatoma.

SUPRASELLAR CHOLESTEATOMAS

Sometimes intracranial cholesteatomas are found in the suprasellar region (Olivecrona,[6] Love and Kernohan). Olivecrona believes that such tumors can be diagnosed before operation on the basis of the following clinical characteristics: (1) the development of a very slowly progressive primary optic atrophy with bitemporal hemianopsia occurring in a young person; (2) the presence of an essentially normal sella turcica with widening of the optic foramina, and pressure absorption of one or both anterior clinoids and of the sulcus chiasmatis; and (3) the complete absence of signs of pituitary insufficiency. Since most of these signs are found with other tumors in this region, the establishment of such a syndrome for cholesteatomas is difficult to accept. Olivecrona believes, however, that the occurrence of these tumors in young people differentiates them from the suprasellar meningiomas, that their growth is slower than is the case with the latter or any other tumor in this

region except the hypophyseal duct tumors, that widening of the optic foramina occurs most frequently with these tumors, and that bone absorption is more characteristic of the cholesteatomas than of other tumors in the suprasellar region. Despite these apparently characteristic features, suprasellar cholesteatomas cannot be diagnosed except at operation. Their features are the features of suprasellar tumors with a chiasmal syndrome which apparently has no specific characteristics. This is illustrated by Case II. (Fig. 2.)

Case II. M. S. was admitted to the University Hospital under the care of Dr. C. H. Frazier on December 8, 1931. She had been well until two years previously when she began to be troubled with headaches which became less frequent and less severe as time wore on. At the same time her eyesight began to fail. This had become steadily worse so that at the time of entrance she had great difficulty in seeing with the right eye and could hardly distinguish light with the left.

Examination revealed bilateral primary optic atrophy. The left visual field could not be taken because of the blindness. The right showed a temporal cut, with some encroachment on the inferior nasal quadrant as well. Otherwise the examination was negative. There were no signs of endocrine imbalance, but there was a history of irregular menses. The basal metabolic rate was minus 16 per cent.

X-ray of the skull revealed a very long and shallow floor of the sella turcica. The sella measured 9×7 mm. and its appearance suggested a suprasellar tumor.

On December 17, 1931, Dr. Frazier performed a right transfrontal craniotomy. A "pearly tumor" was found above the sella turcica, more on the right side. This was removed almost completely.

Histologic study revealed a typical cholesteatoma. The capsule was well-defined. The epithelial layer was several layers thick with a bottom layer of cuboidal cells sitting on a heavy basement membrane. Above these lay three to four layers of cells having no definite arrangement but lying at right angles to the basement layer. The cytoplasm of these cells merged with that of those adjacent and was poorly defined. Keratohyalin granules could be made out in the basement layer of cells. In addition there was a clearly defined stratum fibrosum composed of parallel layers of fibrous tissue. The

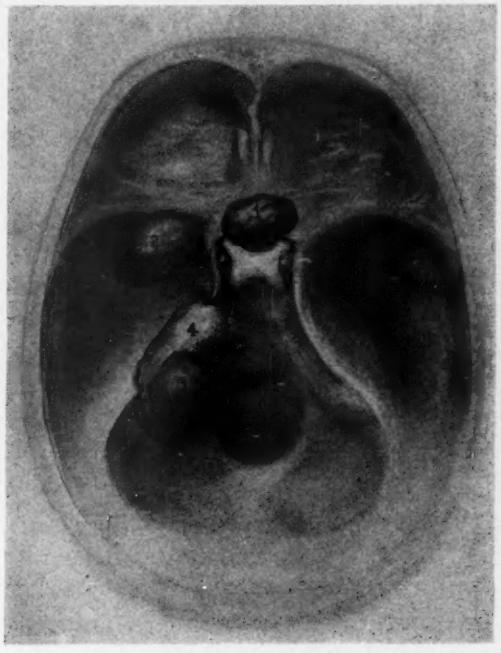

Fig. 2. A composite picture to show the position of the cholesteatomas at the base of the brain in this series. 1, suprasellar (Case II). 2, sphenoid ridge or parasellar (Case III). 3, cerebellopontine angle (Case IV). 4, parapontine (Case V).

stratum cellulosum with its large polyhedral cells was seen plainly.

The patient made a good operative recovery. The vision in the left eye never returned, but the right visual field widened out and the vision increased to $\frac{3}{100}$. She did well until 1935 when she developed recurring blindness in the right eye and improved vision in the left. Operation was advised, but was refused.

This case occurred in a young girl of fourteen and in this respect conformed to the experience of Olivecrona. In all other respects, however, only the signs of a chiasmal syndrome enabled the establishment of a diagnosis of suprasellar tumor.

Suprasellar cholesteatomas are usually small tumors confined to the suprasellar region, but they may become very large and extend into the adjacent middle fossa (Love and Kernohan). Their relation to the optic chiasm does not differ from

other types of suprasellar tumor. They lie under the chiasm, pushing it up, the optic nerves straddling the tumor. While Olivecrona states that bone absorption and dilatation of the optic foramen is seen in these tumors, I am unable to confirm this, either in the single case reported in this series or in the experience of others.

PARASELLAR CHOLESTEATOMAS

One of the more usual situations of cholesteatomas within the skull is in the parasellar area either on the lesser or greater sphenoidal wings. (Fig. 2.) These might be regarded essentially as cholesteatomas of the middle fossa which happen to be located on the sphenoid ridge. Indeed it is not unusual for them to extend into the middle fossa from the ridge just as do other tumors in the same area. The following case illustrates some of the features of a cholesteatoma of the sphenoid ridge:

Case III. S. L. entered the University Hospital on June 18, 1931, under the care of Dr. C. H. Frazier. She had been subject to headaches for the past eighteen years, but these were very rare, coming not more often than once a year. However, they lasted for one to six weeks, and were often associated with nausea and vomiting. About six months before entrance she had a severe headache over the left forehead, eye, and temple. This lasted for three months. Just before its onset she noticed her vision was failing and that it was worse in the left eye. Following the removal of several teeth she became completely blind in the left eye, and developed drooping of the left eyelid. After three months, the headache vanished until five weeks before entrance, although the ptosis persisted. The headache lasted until the time of entrance.

About one year before entrance she had what seemed to be typical uncinate attacks during which she smelled old burning rags. She had hallucinatory experiences in her left visual field, during which she saw figures of people and stones of different colors.

Examination at this time revealed Argyll-Robertson pupils, bilateral primary optic atrophy, a left external rectus weakness, a left trochlear paralysis, ptosis of the left eyelid, and pain in the first division of the left trigeminal nerve. The left visual field was contracted, but there seemed to be a much more pronounced cut in the temporal portion of the field. The blood Wassermann was negative. *X*-ray of the skull and sella was negative.

The patient insisted on leaving the hospital before a final diagnosis was made. She returned in April 1935 with the story that for four years she had been well except for mild headaches. The vision in her right eye was good enough to read with, but the left eye was blind. Since there was a severe recurrence of her headache before entrance she returned for observation. Examination at this time revealed a moderate exophthalmos in the left eye, ptosis of the left eyelid, a left external rectus palsy, and a blurring and papillitis of both optic nerve heads. *X*-ray of the skull at this time showed a well-circumscribed mass just posterior and to the left of the sella turcica. This mass had a calcified periphery.

On March 26, 1935; Dr. C. H. Frazier performed a left temporofrontal craniotomy. A tumor was found on the lesser wing of the left sphenoid bone, extending back into the middle fossa. It was attached to the ridge. A large part of the tumor was removed.

After operation the patient did quite well, but she had a rapid recurrence of symptoms and died in May 1935. No autopsy was obtained.

Histologic study of the tumor showed it to be a cholesteatoma. No capsule was found in the many fragments of tissue removed. However, the large polyhedral cells of a cholesteatoma were seen everywhere in the tissue and this, plus the gross appearance, made a diagnosis of cholesteatoma quite justified.

The trochlear, abducens, and trigeminal paralysis on first examination indicated a parasellar lesion. This was confirmed on second admission by the development of partial left oculomotor paralysis, and exophthalmos of the left eye. The visual fields were of no help because of the loss of vision in one eye, but the uncinate fits were of great value in indicating a lesion adjacent to the uncus region. None of these signs were in any way different from those found in other tumors of this region. The calcification of the

tumor had no features which could be regarded as in any way specific.

That the parasellar area is one of the more common sites of location of the cholesteatomas is shown by the fact that in 142 such tumors collected from the literature by Mahoney,[7] forty-four were in the parasellar or parapituitary region. Mahoney's parapituitary cases include probably not only the parasellar but also the suprasellar cases. He found no evidence of a characteristic syndrome for cholesteatomas in this region.

PARAPONTINE CHOLESTEATOMAS

Among the parapontine cholesteatomas may be included tumors of this type which lie in the cerebellopontine angle as well as those which lie in juxtaposition to the pons outside of the angle. (Fig. 2.) Since there are not a few tumors which lie in relation to the pons outside of the angle, it is probably wiser to accept the term parapontine (Mahoney) than to include them all among the cerebellopontine tumors. The cerebellopontine angle is one of the favorite sites of the cholesteatomas. One of the eight cases which I record was found in this location (Case IV), and another along the pons (Case V).

Case IV. R. D. entered the University Hospital under the care of Dr. C. H. Frazier on August 26, 1932. She had had difficulties in hearing with the left ear since 1925, about seven years before entrance, which became gradually worse until she could no longer hear with this ear. About the same time she developed tinnitus in the left ear, and then bilaterally. It was worse in the right ear and had become quite constant. For four years she had been troubled with dizziness especially on rising in the morning, induced by any change of position. About three years before entrance she noticed inability to coordinate the left arm and leg and found that these limbs were weak. Thickness of speech, severe occipital headaches, and dimness of vision completed the clinical picture.

Examination revealed a spontaneous horizontal, vertical, and rotary nystagmus, a diminished left corneal reflex, early evidences of a left peripheral facial palsy, dysmetria and dyssynergia of the left arm, a reeling gait with falling to the left, unsteady station, and left-sided loss of cochlear function. There was 1D papilledema in each eye. The Barany findings were typical of a cerebellopontine angle lesion. *X*-ray of the skull revealed nothing of interest.

A suboccipital craniectomy was performed on August 27, 1932 by Dr. F. C. Grant. A cholesteatoma was found in the left cerebellopontile angle and was removed in toto except for a small piece of capsule which was attached to the trigeminal nerve.

Histologic study revealed a typical cholesteatoma. There was a typical capsule, composed of a basal layer of cells with large vesicular nuclei and a roomy cytoplasm containing basophilic staining granules of varying sizes. There were two or three layers of cells about the basal layer. Their structure was similar to those of the basilar layer, but they tended to become flatter as one approached the surface. There was a well-defined stratum fibrosum and granulosum.

The next case is most unusual because of its great extent. (Fig. 2.) This tumor covered the left side of the brain stem, compressing both the pons and medulla extending through the incisura beneath the left temporal lobe. Despite its size, it produced relatively few signs.

Case V. K. M. entered the University Hospital March 30, 1936, under the care of Dr. C. H. Frazier. About three years previously she had developed a left Bell's palsy which apparently persisted. Two years later she noticed staggering which had become progressively worse, and for three months she had been troubled with diplopia. She had never had headaches or vomiting.

Examination revealed a left oculomotor weakness, an absent left corneal reflex, deviation of the jaw to the left, weakness of the left abducens nerve, a peripheral left facial paralysis, deafness in the left ear, immobility of the pharynx, weakness of the right hand and hyperactive reflexes. Visual field studies revealed enlargement of the blind spots. Barany studies revealed a brain stem lesion on the left side, probably in the angle. Vestibular and cochlear responses were absent on the left side.

On April 2, 1936, Dr. S. N. Rowe performed a suboccipital craniectomy. In the left cere-

bellopontine angle was a large tumor which extended from the upper end of the spinal cord along the brain stem beyond the tentorium,

Fig. 3. Cholesteatoma in fourth ventricle. The medulla has been pinned back in order to show the tumor. (Case vi.)

disappearing beneath the left temporal lobe. All the tumor in the posterior fossa and part of that portion in the middle fossa were removed. She made a good recovery but there was no improvement in her facial paralysis.

Histologic study revealed a cholesteatoma. There was no capsule, but there were many polyhedral cells, and this, with the typical gross appearance of a pearly tumor, identified the growth as a cholesteatoma.

Cholesteatomas in the parapontine region are more numerous than in any other part of the brain or brain stem. Of the 142 cases collected by Mahoney, fifty-three were in the parapontine region compressing the pons either anteriorly or in the cerebellopontine angle. There is nothing to differentiate these neoplasms clinically from other tumors in the angle. They give a history of a typical cerebellopontine angle tumor.

FOURTH VENTRICLE CHOLESTEATOMAS

In a small number of instances cholesteatomas are found within the fourth ventricle. Mahoney found fifteen such instances among 142 cholesteatomas. The following case (Fig. 3) illustrates the features of a cholesteatoma in this location:

Case vi. M. H. was admitted to the University Hospital August 1, 1932, under the care of Dr. C. H. Frazier. She had been well until five months before entrance when she fell down the stairs. Following this she noticed weakness of the right leg. For several months before her fall, however, she had observed that she was unable to use her right hand and arm well; she had great trouble in writing, in threading a needle, and in knitting. Delicate movements involving the right hand were difficult to perform. For about five months there had been weakness of the right arm. One month before entrance her gait became unsteady so that she had to hold on to the furniture for support. She noticed a tendency to fall to the right in walking. Diplopia developed a month before entrance into hospital.

Examination revealed horizontal and vertical nystagmus, dyssynergia of all the limbs, more marked on the right side, a staggering gait with reeling toward the right side, slight drooping of the lower part of the right face, and bilaterally hyperactive reflexes. There was 1.5D of choking in each eye.

X-ray of the head revealed severe atrophy of the dorsum sellae with retention of the posterior clinoids, increase in size of the sella turcica (11 × 9 mm.), and erosion of the sellar floor on the right side.

A suboccipital craniotomy was performed on August 12, 1932, by Dr. Francis C. Grant, and a fourth ventricle cholesteatoma was revealed. The patient collapsed on the table before any efforts could be made to remove the tumor.

Histologic study revealed a typical cholesteatoma with a capsule composed of several layers of epithelial cells, the basement layer composed of large cuboidal cells containing many basophilic granules in the cytoplasm. The stratum fibrosum and cellulosum were easily made out.

The diagnosis of a fourth ventricle tumor is exceedingly difficult. Frequently the signs are obscure and are those only of increased intracranial pressure. Some times, as in Case vi, the signs are predominantly cerebellar in type, a fourth ventricle tumor being disclosed only after a posterior fossa exploration. Here there

were no signs which could be regarded as specifically indicating a cholesteatoma. The clinical signs pointed to a cerebellar tumor; that it was a fourth ventricle cholesteatoma was disclosed only after exploration.

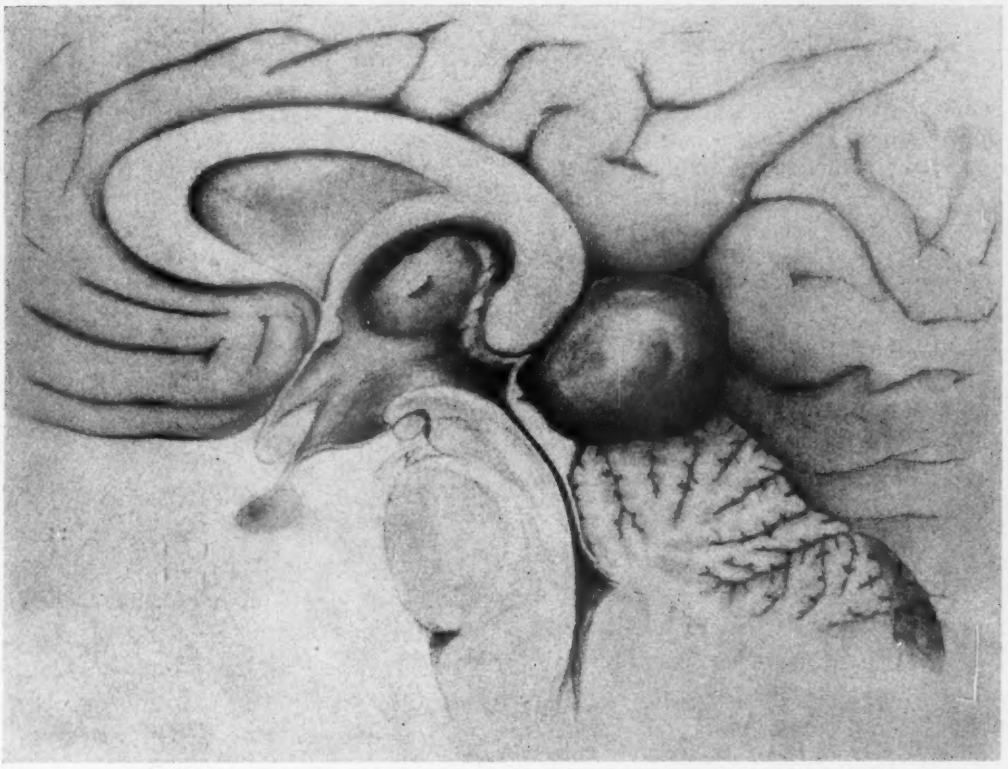

Fig. 4. A large cholesteatoma in the pineal recess. (Case vii.)

Cholesteatoma of the Pineal Recess

Cholesteatomas in this region are very uncommon. None are mentioned among the 142 cases culled from the literature by Mahoney. The following Case (Fig. 4) illustrates the features of a tumor in this region:

Case vii. E. M. was admitted to the University Hospital September 5, 1934, under Dr. C. H. Frazier. About two years before entrance he began to have difficulty in walking, noticing a tendency to stagger to the right. He had had headaches for the same length of time, and vision had been failing for about a year. His difficulty in walking became progressively worse and finally necessitated hospitalization.

Examination revealed a combination of mental and cerebellar signs. The pupils reacted sluggishly to light. Dyssynergia was present in the right arm. There was an intention tremor of the right hand, the gait was very unsteady and on a wide base. The memory for recent events was poor and the patient was very facetious.

The fundi showed 1.5–2 diopters choking on the right and 1 diopter on the left. There was post-papillitic optic atrophy. Vision was lost on the right and was $\frac{6}{60}$ on the left.

The *x*-ray showed evidences of increased intracranial pressure due to posterior fossa tumor. Convolutional atrophy, enlargement of the sella turcica with loss of the dorsum sellae, and some depression of the sellar floor were present. The pineal body was displaced posteriorly.

Ventriculogram was performed on September 13, 1934, because of the difficulty in localizing the process clinically. Air studies revealed dilatation of the lateral and third ventricles but no air was seen in the iter or fourth ventricle. It was decided that there was a block in the region of the third ventricle, possibly due to a pinealoma.

Operation. On September 13, Dr. R. A. Groff performed a subtemporal decompression in order to give some relief from pressure symptoms and to permit an approach to the pineal recess.

On August 20, Dr. S. N. Rowe performed a second operation. A right temporofrontal approach was made. Under the corpus callosum, in the pineal recess was found a tumor which had the typical appearance of a cholesteatoma. The tumor measured about 5 cm. in all diameters. The patient lingered on for a few weeks after operation, but finally died.

Histologic study of the tumor revealed a cholesteatoma. There was a well-defined epithelial capsule composed of three or four layers of cells. Their structure was similar to those of the preceding case. All the other layers of a cholesteatoma were present. There was a heavier fibrous layer than in some of the other tumors, and large number of lymphocytes.

Here too there was nothing to permit a preoperative diagnosis of cholesteatoma. The signs present in this case were obscure at best and did not indicate a process localized in the region of the pineal body. Only after air studies was the location of the tumor revealed.

CHOLESTEATOMA OF THE SKULL

Occasionally cholesteatomas arise within the bones of the skull between the inner and outer tables. Mahoney has gathered twenty-three such cases from the literature. The following example of this type has been reported previously (Alpers and Harrow[8]).

Case VIII. This woman of 52 had a cholesteatoma of the right occipital bone. She had had symptoms for twelve years, chiefly visual disturbances, headache, and nausea. She was operated on and a large cholesteatoma removed from the right occipital bone. It had produced a severe bulging of the inner table, some erosion of this table, and compression of the brain. It was entirely extradural and was removed completely. She made an excellent recovery.

The subject of the diploic cholesteatomas has been reviewed on several occasions, especially by Cushing,[9] Alpers and Harrow, and Bucy.[10] Cholesteatomas arising within the skull bones have been found in the frontal, temporal, occipital, parietotemporal, and temporo-occipital regions. They grow very slowly, and remain extradural throughout their course. They usually cause an expansion of the inner table of the skull and a compression of the underlying brain substance, but they may cause an erosion of the outer table and infiltrate the tissues beneath the scalp. This is an uncommon feature, but it has been found in a few instances.

Diploic cholesteatomas give rise to very few signs until they compress the brain substance, and then the signs are only of the vaguest sort. The one certain way of diagnosing these tumors is by *x*-ray, which shows a separation of the tables of the skull, thinned by the pressure of the expanding tumor. The inner table usually suffers more than the outer. Sometimes one finds erosion of this table. Usually there is bone absorption and destruction in the region of the tumor, sometimes of a severe degree. The Roentgen picture, as Cushing has said, resembles very much an old craniotomy defect.

DISCUSSION

Incidence. Cholesteatomas are relatively rare brain tumors. They represent 0.6 per cent of verified brain tumors in Cushing's series. In Frazier's series of 758 verified cases, there were eight cholesteatomas representing 0.13 per cent. They may occur at any age. The ages in the eight cases reported in this paper varied from 14 to 58. The average age in the 142 cases gathered by Mahoney was 35, the extremes being from 1½ to 78. There is no preponderance in either sex.

Pathology. The story of the cholesteatomas has been told many times. Good accounts of their pathologic characteristics have been given by Critchley and Ferguson, Mahoney, and Bailey.[11] As may be seen from the cases reported and from those gathered from the literature, cholesteatomas may be found in relation to

any part of the cerebral hemispheres, the suprasellar region, the sphenoid bone and middle fossa of the skull in the parasellar to parapituitary area, the pons (parapontine), the fourth ventricle, the bones of the skull, and rarely within the spinal canal. They are most frequently encountered in the parapontine region either in the cerebellopontine angle, where they seem to like to dwell, or in relation to the more anterior portions of the pons. Their next most frequent site is in the parasellar region in relation to the lesser wing of the sphenoid bones or the structures lying close to the sella turcica. The diploic and fourth ventricle cholesteatomas follow them in frequency.

The cholesteatomas are well-defined growths which are discretely separated from the adjacent brain tissue. They practically always lie outside of the brain substance. In the few instances in which they have been described as lying within the brain tissue, the cerebrum and pons, it has seemed definitely true that they had burrowed their way into the brain from without.

The cholesteatomas in the suprasellar area are confined pretty largely to this area. Those which lie on the sphenoid ridge tend to grow into the middle fossa and to burrow under the temporal lobe, whereas the parapontine tumors may sometimes spread far beyond the confines of the cerebellopontine angle and extend anteriorly along the brain stem (Alpers, Mahoney).

Great emphasis has been placed by some (Bailey), on the intimate relation of these tumors to the meninges. In none of my cases was there an adherence of the tumors to the arachnoid, pia, or dura. The tumors have a good capsule. Their glistening, pearly-white, mother of pearl appearance has been too often described to bear repetition. Beneath the capsule are concentric layers of this glistening tissue, giving the appearance of an onion-like arrangement, and the concentric layers may be separated, carefully, in onion-like fashion. The tissue is very friable and brittle, easily broken even with the most delicate handling.

The microscopic structure of the cholesteatomas is quite constant. The division by Bailey into the following four layers from without inward is in my experience quite satisfactory: stratum durum, granulosum, fibrosum, and cellulosum. The stratum durum is a fibrous layer which frequently contains hematogenous elements, probably from secondary or symptomatic inflammation. It is quite homogeneous in appearance. The stratum fibrosum is composed of many layers of homogeneous material. The stratum cellulosum consists of masses of polyhedral cells of the typical cholesteatomatous variety. The stratum granulosum is composed of epithelium of a modified squamous nature. It has a basilar layer of cuboidal cells in which one can frequently identify keratohyaline granules. Above this are several layers of cells composed of squamouslike epithelium in which one can sometimes identify intercellular bridges.

It is said that the diagnosis of a cholesteatoma depends upon the identification of this epithelial portion of the capsule. Although this is true in general, I have seen cholesteatomas which at operation had the typical appearance of such tumors grossly, but which were removed in pieces and in which a careful search of all the fragments failed to reveal the capsule. All the other elements of the cholesteatoma were present and in such instances I have felt justified in making a diagnosis of a cholesteatoma even in the absence of a capsule. It seems inconceivable to me that a degenerated hypophyseal stalk tumor, a gliomatous cyst, or a brain abscess which has undergone degeneration can become so completely metamorphosed as to give the typical gross appearance of a cholesteatoma. Where cholesteatomas are removed piecemeal, it is quite possible that the capsule may become disintegrated in the process of fixation and dehydration. For this reason I believe that the rule that the

capsule must be found for proper identification of these tumors cannot be too rigidly enforced.

Clinical Features. I know of no way in which a cholesteatoma may be diagnosed preoperatively. There is no characteristic clinical picture in any of the locations in which these tumors are prone to appear. Olivecrona has mentioned certain features which seem to characterize the suprasellar cholesteatomas, but these are not definite enough to distinguish them from other tumors in the suprasellar region.

Mahoney calls attention to the frequent occurrence of mental symptoms in cholesteatomas of the parapontine group, but this can hardly be regarded as a feature of diagnostic value. A similar claim has been made in the case of the cerebral lipomas, often characterized by the presence of mental symptoms. These in themselves can have little value in the diagnosis of a cholesteatoma, though they may direct suspicion toward such a lesion. That the mental changes may be of more than passing interest, however, is shown by the experience of Love and Kernohan, who found a large number of cholesteatomas accompanied by such symptoms. They stated that, "a congenital intracranial dermoid or epidermoid should be suspected in any case in which mental disturbance is associated with headache that has been present for a long time and suggests increased intracranial pressure."

The duration of symptoms in my cases varied from five months to eighteen years. In two cases symptoms had been present for fourteen and eighteen years, respectively (weakness of the right leg in the first instance and headache in the second). The shortest duration of symptoms was found in the fourth ventricle cholesteatoma, as one might expect. A tumor in this region could not exist for long without producing symptoms of some sort.

Treatment. Surgical removal of these tumors offers the only sure method of relief of symptoms. In the eight cases reported in this paper, six made good recoveries, although in one recurrence occurred after a period of five years. Of the 142 cases which Mahoney collected from the literature, 70 per cent died without operation. Of the remaining 30 per cent only one-third survived the operation. Mahoney calls attention, however, to six cases with good recovery reported by Cushing and the recent report of Love and Kernohan in which twelve of fifteen cases recovered, indicating that with more modern methods of brain surgery the possibilities of cure in these cases is good.

If the tumor is removed completely, with the capsule intact, there should be no recurrence. Cholesteatomas are often so situated that they are subject to complete removal. Even in those situated at the base of the brain, it is often possible to remove the tumor in large part, if not completely. Recurrence takes place whenever the capsule is not completely removed, but if the tumor cannot be removed completely, it should be taken out piecemeal. This can be done quite readily since these tumors are soft and easily curetted. While the operative score in the past in these tumors has been none too good, it is probable that with our present improved techniques it will be much better.

SUMMARY

Cholesteatomas may occur in any part of the cranial vault and in relation to any part of the brain. They have been found in relation to the frontal, temporal, parietal, and occipital lobes and in one instance reported here a large parietal cholesteatoma was operated on. They lie outside the brain substance, grow slowly, and may excavate a large area of brain tissue in making a bed for the tumor. At the base of the brain they are found in the suprasellar region, next to the pons (parapontile), in the cerebellopontile angle, and in the fourth ventricle. In none of the areas are these tumors characterized by a typical history or by characteristic findings which enable one to make a preoperative

diagnosis. They do, however, give the signs of a tumor in the areas affected. They may be diagnosed therefore only at operation. Only the skull cholesteatomas may be diagnosed before operation, since they have a characteristic roentgenographic picture. Operation of these cases offers good hope of cure provided the tumor and all its capsule can be removed intact. If the capsule is not removed recurrence is certain.

REFERENCES

1. Love, J. Grafton, and Kernohan, James W. Dermoid and epidermoid tumors (cholesteatomas) of central nervous system. *J. A. M. A.*, 107: 1876 (Dec. 5) 1936.
2. Nehrkorn. Ein Fall von meningealer Perlgeschwulst. *Beitr. z. path. Anat. u. allg. Path.*, 21: 73, 1897.
3. Kakeshita, T. Zur Pathologie der Hirn Cholesteatom. *Arb. a. d. neurol. Inst. a. d. Wien Univ.*, 27: 327, 1925.
4. Critchley, MacDonald, and Ferguson, Fergus R. The cerebrospinal epidermoids. *Brain*, 51: 334, 1928.
5. Learmonth, J. R., and Kernohan, James W. Three cases of epidermoid cyst of the brain. *S. Clin. North America*, 11: 853 (Aug.) 1931.
6. Olivecrona, H. On suprasellar cholesteatomas. *Brain*, 55: 122, 1932.
7. Mahoney, W. Epidermoids of the central nervous system. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 155: 416 (May) 1936.
8. Alpers, Bernard J., and Harrow, R. Cholesteatoma originating in the skull bones. *Am. J. Surg.*, 18: 51 (Oct.) 1932.
9. Cushing, Harvey. A large epidermal cholesteatoma of the parieto-temporal region deforming the left hemisphere without cerebral symptoms. *Surg., Gynec. & Obst.*, 34: 557, 1922.
10. Bucy, P. Intradiploic epidermoid (cholesteatoma) of the skull. *Arch. Surg.*, 31: 190 (Aug.) 1935.
11. Bailey, P. Cruveilhier's tumerus perlées. *Surg., Gynec. & Obst.*, 32: 390 (Oct.) 1920.

TRAUMATIC INJURIES TO THE HEAD

A STUDY OF 200 CONSECUTIVE CASES

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THE problem of traumatic injuries to the head necessarily includes injuries to the scalp, skull, and the brain with its membranes and blood vessels. These injuries are produced in various ways, but violence is the outstanding feature.

Table 1 presents our series of 200 head injuries from an etiologic aspect and at the same time indicates the degree of associated violence. This clinical material was taken from the Boice-Willis Clinic. The cases were treated by members of the staff, surgical and medical, until a few years ago when the problem was turned over to one person.

TABLE I
ETIOLOGY

Cause	No. of Cases	Deaths
Auto	129	20
Manual violence	23	2
Mule kick	6	1
Falls	8	1
Falls from mule or horse	3	
Motorcycle	2	1
Industrial accident	3	
Bicycle hitting head	2	
Water tank explosion	1	1
Accidental rifle shot	1	1
Thrown as mule ran away	1	1
Baseball	2	
Wagon tongue hitting head	1	
Hitting head on shelf	1	
No history	17	4
Total	200	32

Scalp and skull injuries unassociated with intracranial involvement are to be considered chiefly from the standpoint of prevention of subsequent invasion of infection into the cranial cavity. The danger of the simple scalp wound lies in its apparent insignificance.[1] Every injury to the head should be thought of as being serious until it can be proved otherwise. A careful history should always be taken, including the manner of the injury and the state of consciousness following the accident. The repair of the wound should also include an investigation of the underlying structures for foreign bodies and for damage to the periosteum and skull. In the absence of skull or intracranial disturbance, the potentially infected wound should be converted into a surgical wound by careful cleaning and débridement, and closed with or without drainage, depending upon its extensiveness. In the preparation of scalp wounds for repair one does well

TABLE II

Skull fractures	102
Suspected skull fractures	30
Proved by *x*-ray, operation, or aural bleeding	72
Of these 72, there were:	
Without cerebral damage	11
With cerebral hemorrhage	20
With gross brain damage	14
Basal	23
Vault	48
Frontal sinus	8
Suture line upset	10
Compound skull fractures	36
(13 died, 9 sequelae)	
Basal	16
Vault	18
Sinus	5
Depressed	22
(5 died, 3 sequelae)	
Compound	13
Operated	13
Parietal	21
(5 died, 9 sequelae)	
Temporal	9
(3 died, 1 sequelae)	
Occipital	6
(No deaths or sequelae)	
Frontal	26
(6 died, 10 sequelae)	

to remember that the patient, in spite of her beauty, can grow hair with greater facility than she can combat infection.

Compound depressed fractures of the skull are frequently associated with injuries to the membranes, brain, or both.

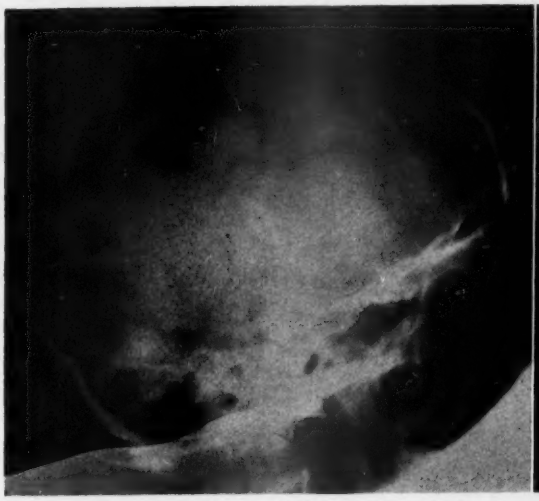

Fig. 1. Compound depressed fracture of skull. Termination in this case was death.

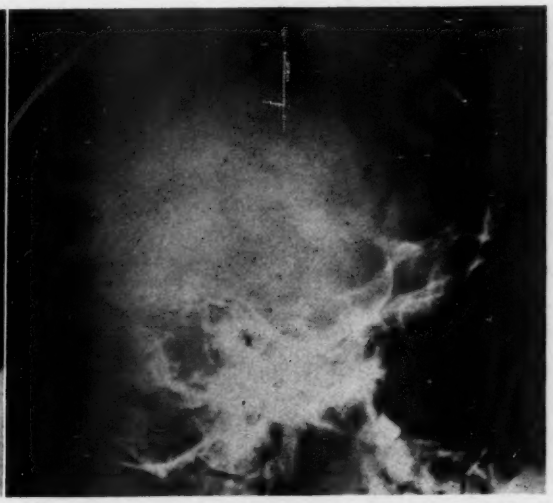

Fig. 2. Compound depressed fracture of skull with extensive bone and brain destruction of the frontal area. This patient recovered without sequela.

Five of the 200 patients here surveyed were admitted to the hospital for scalp wounds.

Simple linear fractures of the vault unassociated with scalp and intracranial injuries are probably no more dangerous than fractures of other bones. The occurrence of uncomplicated linear fractures is shown in Table III. Linear fractures of the temporal bone have as their principal danger, provided that they do not extend into the base, the possibility of a rupture of the middle meningeal artery or some of its branches.

Table III

Linear fractures	13
(No deaths, 8 sequelae, 61.5 per cent)	
Intracranial damage	12
Sequelae	7

Simple depressed fractures, not of the massive type sufficient to produce compression per se, are of importance depending upon their locality; i.e., a depressed fracture over a silent area of the cortex may be insignificant, while a depressed fracture over the motor area may present an entirely different picture.

The question of hemorrhage, actual brain destruction, and infection add to the gravity of these injuries, as does their location. Basal fractures are usually compound and are dangerous because they present open avenues to intracranial infection through the ears, nose, mouth and sinuses, in addition to blood vessel damage with resulting hemorrhage. Table IV indicates that hemorrhage and brain damage, and not infection, have been responsible for the deaths in this series. While these statistics show that there is a definite relationship between skull fracture and severe brain damage, it must be borne

Table IV

Basal skull fractures	41
Suspected	18
Proved	23
Fate of the 41 basal skull fractures:	
Died	24
(58.5 per cent—corrected mortality of 44.1 per cent)	
Gross grain damage	6
Cerebral hemorrhage	17
Compound	16
Sequelae	7
Slightly deafened	3
No meningitis	
No rhinorrhea	

in mind that "a fatal termination may ensue in consequence of cerebral damage, in the absence of bone injury, or wound of scalp."[2]

Extradural hemorrhage, "the thief in the night of traumatic head injuries," does not offer a great deal of difficulty from a diagnostic standpoint when the symptoms are typical. Verbrugghen[3] reports that in about 10 per cent of the cases coming to autopsy, extradural hemorrhage is regarded as the principal cause of death. In some cases there is no "lucid interval." The unilateral dilatation of the pupil occurs after a primary contraction of the pupil when it is due to extradural hemorrhage; when the patient is seen late, both pupils may be equally dilated. Unilateral dilatation of the pupil, present from the moment of injury, is caused by a damage to the third nerve. Progressive coma and descending contralateral convulsions, spasticity and paralysis, are thought to be the most reliable diagnostic signs of this condition.

That the occurrence of this injury is not dependent upon the presence of a skull fracture or a torn dura, was demonstrated by the author in the performance of a medicolegal autopsy.

Middle meningeal hemorrhage, depressed fractures, compound or not, subdural hematoma, and scalp lacerations require surgical treatment. Table v gives the number of cases operated upon and the type of operation performed. The importance of the correct management of scalp lacerations per se is well recognized, but will be omitted here in order to give more consideration to craniocerebral injuries.

TABLE V

	Cases
Surgical treatment of head injuries	19
Raised bone	9
Active hemorrhage checked	1
Subdural clots removed	2
Brain irrigations	3
Removal of depressed bone	5
Irrigation* of brain	1
Debridement of brain	1
Craniotomy	
To control hemorrhage	1
Exploration for abscess	1
Removal of blood clot	1

* The treatment referred to as irrigations was in reality débridement inasmuch as macerated brain was washed and sucked away.

Shock is generally present to some degree in craniocerebral injuries and demands immediate intelligent attention lest the patient die before the injury can be treated. Heat is the most effective single method.[4] In combating low blood volume in shocked head cases, it is to be remembered that there will be edema of the brain, following the shock. Hypertonic glucose, or preferably sucrose, 50 c.c. of a 50 per cent solution, will replace the volume. Acacia and blood should be used if necessary. Stimulants are best omitted unless hemorrhage can be excluded. "Recovery from shock without hemorrhage is usually prompt unless the injury is so severe that death occurs in a short time."[4] Extracranial hemorrhage must be checked while the shock is being treated.

Compound fractures of the skull, with or without depression, where there are spicules of bone, dirt, etc., require operation as soon as the shock has been combated. Débridement is the best procedure. Where possible, skull fragments are replaced. (Fig. 2.)

Elmer and Boyland[5] state that "rapid immediate decompression with adequate supportive treatment is the procedure of choice in children with depressed fractures." This has been our experience also.

One of the patients included in this series was operated on for subdural hematoma. The operation was performed two weeks after his injury when he was admitted into the hospital in a state of rapidly progressive coma. The operation consisted of saline irrigations through trephine openings. Bilateral exploration of the dura was performed. (Fig. 4.)

None of the cases in this series received a subtemporal decompression for the relief of increased intracranial pressure.

Hemorrhage for a ruptured middle meningeal artery should be checked as

soon as it is diagnosed. The treatment is surgical.[6]

X-ray examinations should not be considered early in the treatment of these injuries, but should be postponed until the patient is out of danger, except where there is a question of extradural hemorrhage.[7] A positive *x*-ray finding of a linear fracture crossing the path of the middle meningeal artery or its branches may be of use and therefore excusable in instances of this kind.

Fig. 3. Rupture of superior longitudinal sinus. Bilateral subdural hemorrhage. This patient had been struck over the vertex with an axe helm and died in fourteen hours.

Fig. 4. Subdural hematoma. Treatment by saline irrigations through trephine openings. Bilateral exploration of the dura. *X*-ray taken one year after recovery.

As long as the patient with a depressed fracture or bloody spinal fluid is holding his own, or is showing improvement under treatment, operation should be postponed for a few days. The patient will have a better chance for recovery.

The postoperative treatment is largely that of combating increased intracranial pressure. Of our 200 cases, 176 were classified as non-surgical. These varied in seriousness from momentary loss of consciousness with apparent complete recovery in a few hours, up to prolonged unconsciousness, two weeks in one instance, with definite evidence of severe structural damage. Many of this group had injuries to other parts of the body. Those unconscious for less than thirty minutes were considered, from an intracranial standpoint, as cases of mild concussion. They were hospitalized for a period which average 4.1 days. (Table VI.) Some of these cases were concussions as defined by Munro,[7] i.e., "a mechanical derangement of molecules within the nerve cells causing momentary loss of function" while the others must have had mild, but definite, brain damage, probably slight edema and congestion. The occurrence of sequelae in 19.2 per cent suggests this.

Table VI

TREATMENT OF CASES OF MILD CONCUSSION

Non-surgical cases	176
Mild concussion	74
Observation* (7 sequelae)	55
Dehydration (7 sequelae)	19
Corporal fractures	12
Ruptured hollow viscus	1
Deaths	0

* Included frequent recordings of blood pressure, temperature, pulse and respiration.

Fifty patients were admitted to the hospital in an unconscious state. These offered the greatest problem. Concussion, delirium, aphasia, stupor, all with or without shock and hemorrhage, were present in this group. Twenty-one had additional injuries. In evaluating these

cases the degree of consciousness is perhaps the most valuable single observation.[6,7] A differentiation between stupor and aphasia is important. Loss of sphincteric control and the presence or absence of the various reflexes are of prognostic value. Negative symptoms are just as important as positive symptoms in that they aid the observer to follow the progress of the case more intelligently. "Hemiplegia and monoplegia, when caused by depressed skull fractures, are present from the moment of injury."[8] The relationship between pulse pressure and pulse rate should be recorded at frequent intervals. These observations, together with a spinal fluid pressure reading, give more information regarding the intracranial state than does the *x*-ray. A study of the eye-grounds is useful after the first twenty-four hours.

The treatment of the unconscious patient should begin from the moment he arrives at the hospital, or ideally as soon as the physician arrives at the side of the patient. Peace and quiet are needed. He should be placed in a warm, flat bed, with his clothes on if necessary. To recapitulate shock is the first consideration. Patients presenting pulmonary edema or who are bleeding from the nose or mouth should be turned on the abdomen and have a pillow placed under one shoulder. At the same time the foot of the bed is elevated to facilitate postural drainage. Treatment based on the assumption that "death from a head injury is due to changes brought about in the physiological relationship within the cranial cavity"[9] is instituted. Increased intracranial pressure, if carried far enough, produces cell death by anoxemia, and anoxemia occurs when the diastolic pressure reaches 40 mm. of mercury.[10]

The patient not infrequently loses or wins his fight during the first twenty-four hours. Every effort should be made to keep the patient going, by helping nature with her heavy burden until she can carry on unassisted. The diastolic blood pressure must be kept up and the intracranial pressure must be kept down. Drugs, the continuance of which might be harmful later on, hypertonic fluids, etc., are permissible during this period. Oxygen through a nasal catheter, sponges for fever and other such treatments may be life saving. While these treatments are under way, such minor details as bleeding ears may be attended to, lest they give trouble later on. Table VII shows the methods used and the results obtained in this series of cases. Intravenous hypertonic glucose solution was used, with dehydration in only a few instances. Dehydration and repeated lumbar punctures were found to be more effective than the other types of treatment mentioned.

TABLE VII
METHOD OF TREATMENT OF SEVERE HEAD INJURIES

	No. of Cases	Percentage
Total cases of non-surgical treatment	93	
Observation	49	52.7
Mortality	..	30.6 (corrected 20.9)
Sequelae	..	26.5
Lumbar puncture alone	12	12.9
Mortality	..	41.7 (corrected 27.3)
Sequelae	..	41.7
Dehydration alone	13	14.0
Mortality	..	15.4 (corrected 7.7)
Sequelae	..	53.8
Dehydration & occasional lumbar puncture	19	20.4
Mortality	..	26.3 (corrected 21.1)
Sequelae	..	36.8
Repeated lumbar puncture and dehydration	15	
Mortality	..	13.3
Sequelae	..	40.0

Fay's adage "when the pulse pressure approaches the pulse rate, that is the time to dehydrate"[10] has been followed, in preference to the old adage "if pulse pressure crosses the pulse rate, that is the time to decompress." The treatment of our recent cases has largely followed the teachings of Fay. Dehydration when

carried too far produces a toxic dehydration.[11] A fat person can stand more dehydration than can a thin person.

Repeated lumbar punctures have been performed upon patients presenting bloody spinal fluid on the grounds the red blood cells produce arachnoiditis with subsequent blockage of the arachnoid pathways and filter.[12] Those patients found to have an increased intracranial pressure at the time of the diagnostic tap, have also had repeated punctures for the purpose of reducing intracranial pressure.

Sucrose, 50 per cent, in 50 c.c. doses, has been used in two cases, one of which was definitely benefited by its use. The late elevation of intracranial pressure seen following the intravenous use of hypertonic glucose has been shown by Masserman[13] not to occur after the use of sucrose, his argument being based upon the fact that sucrose is not extracted from the circulation into the tissues, and that it induces a marked diuresis. Hahn and his associates have found from clinical experience with twenty-five cases of acute brain injury that sucrose given intravenously replaces glucose for osmotic therapy.[14]

The problem of sedation is sometimes great. When possible, the bromides, barbiturates, and paraldehyde should be used and not opiates. We have considered morphine and H. M. C. necessary in some instances. A part of the objection to this drug can be overcome if the patient is carefully watched.

Table VIII
PROGNOSTIC FACTORS

	No. of Cases	Deaths	Per Cent Mortality
Convulsions on admission	10	4	40
Unconscious on admission	50	20	40
Aural bleeding	17	8	47.1
Right aural bleeding	..	..	66.7
Left aural bleeding	..	..	33.3
Bilateral aural bleeding	..	..	50
Fractured skull	102	31	30.3
Bloody spinal fluid	25	12	48.0

Table IX
INCIDENCE AND TYPE OF SEQUELAE

Cases followed after discharge	74	
Well	21	28.4 per cent
Mild sequelae	25	71.6 per cent
Moderate sequelae	6	
Severe sequelae	22	

The prognostic factors, and the incidence and type of sequelae are shown in Tables VIII and IX. Mild sequelae were evidenced by headache, dizziness, or slight nervousness. Moderate sequelae were considered irritability and loss of enthusiasm. Severe sequelae were indicated by personality change, convulsions, blindness, insanity, etc.

Table X shows the mortality rates, corrected and uncorrected. The corrected mortality rate excludes deaths occurring in the first twenty-four hours.

Table X
MORTALITY RATES

	Gross Rate, Per Cent	Corrected, Per Cent	Further Corrected, Per Cent
Entire series—200 cases	16.0	9.9	4.9
113 cases of past two years	12.4	8.0	4.7
Mild head injuries—90	0		
Severe injuries—110	29.1	18.8	10.9
55 cases of past two years	25.5	17.0	10.2
Cases under 12 years	11.9		
13–21 years	8.7		
22–35 years	14.3		
35–50 years	21.9		
Over 50 years	30.4		

SUMMARY

1. A series of 200 cases of head injury has been studied.

2. The treatment has been surgical in nineteen cases and non-surgical in 181 cases.

3. The lowest mortality, in the seriously injured, occurred in the cases treated by repeated lumbar punctures and dehydration.

4. The most severe sequelae occurred in those cases having the most serious injuries.

5. The mortality can be reduced by the application of therapy based on physiologic principles and careful bedside observation.

6. No case should be considered as lost from the moment of injury, although this is true in a certain definite number of instances through virtue of the fact "that therapy has little influence on those cases in which actual brain damage is primarily responsible for the clinical picture."

REFERENCES

1. Morton, H. M. A scalp wound and its sequela. *J. Roy. Med. Corps*, 66: 267–271, 1936.
2. Jackson, Harvey. Head Injuries. The Practitioner, 138: 181–201, 1937.
3. Verbrugghen, Adrien. Treatment of head injuries. *Illinois M. J.*, 69: 252–256 (March) 1935.
4. Davis, L. The treatment of craniocerebral injuries. *Michigan Med. Soc.*, 24: 487–496 (Aug.) 1935.
5. Elmer, R. F., and Boyland, C. E. Skull fractures in children with special reference to depressed fracture and cerebral laceration. *Illinois M. J.*, 52: 455–458, 1932.
6. Dandy, W. E. The treatment of injuries of the head. *Pennsylvania M. J.*, 39: 755–759 (July) 1936.
7. Munro, D. The diagnosis, treatment and immediate prognosis of cerebral trauma. An introductory study of 1,494 cases. *New England J. Med.*, 210: 287–294 (Feb. 8) 1934.
8. Brennan, J. P. Acute head injuries. *Med. Rec.*, 143: 523–526 (June) 1936.
9. Fay, Temple. Head injuries, their management and treatment. *J. South Carolina M. A.*, 31: 233–243 (Dec.) 1935.
10. Fay, Temple. The treatment of acute and chronic cases of cerebral trauma by methods of dehydration. *Ann. Surg.*, 101: 76–132 (Jan.) 1935.
11. Earl, R. Treatment of head injuries. *Minnesota Med.*, 18: 521–525 (Aug.) 1935.
12. Bagley, Charles. Functional and organic alterations in the cerebral nervous systems: experimental data. *Arch. Surg.*, 17: 18–81 (July) 1928.
13. Masserman, J. H. Effects of the intravenous administration to hypertonic solutions of sucrose, with special reference to the cerebrospinal fluid pressure. *Bull. Johns Hopkins Hosp.*, 57: 12–21 (July) 1935.
14. Hahn et al. Clinical experience in the use of sucrose instead of dextrose. *J. A. M. A.*, 108: 773–776 (March 6) 1937.

SELECTION OF CASES FOR TRANSURETHRAL RESECTION*

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ANY discussion of the selection of cases for transurethral resection must be variable, since the attitude of a surgeon beginning in this work must of necessity be entirely different from that of operators who have supervised many hundred cases; such men as Alcock, Bumpus, Davis and Thompson are resecting all types of obstructive lesions. It appears, therefore, that the selection of cases depends entirely upon the individual operator's experience and his attitude toward the position of transurethral resection in the operative field.

Almost everyone was caught in the wave of enthusiasm that swept the country in 1933, in which operators without sufficient experience attempted the resection of the enormous type of prostatic enlargement which the beginner should reject without hesitation. It was inevitable that in our first fifty cases the greatest difficulties and the highest mortality were encountered.

In the selection of cases it is essential to begin with the small median bars or median lobes requiring the removal of only the minimum amount of tissue. As the operative technique improves the smaller types of benign adenomas may be attempted. In two of the patients encountered a generalized fibrosis of the entire bladder neck and posterior urethra was present. Resection in this type of case has not proved entirely satisfactory. The removal of tissue under these circumstances is difficult with the punch instrument due to the difficulty of engaging the hard, resistant fibrous tissue. It is manifestly impossible to remove all of the fibrosis by this method, so that transurethral operations in these cases must be followed by dilatation of the posterior urethra. Resection will relieve the urinary retention, but frequency of urination is likely to persist.

Careful study is required at first to determine the position of the obstructing tissue. Enlargements of the anterior lobe and the anterior portions of the lateral lobes must not be overlooked, since failure to remove tissue in these positions may frequently account for poor results. At the present time, therefore, I am resecting all types of benign obstructive lesions with the exclusion of the very large prostates (those estimated to weigh more than 100 Gm.). Since it is possible under the present set-up to remove between 20 and 30 Gm. of tissue at one sitting without great difficulty, it is best to select cases in which obstruction can be relieved with the removal of 60 Gm. of tissue or less. Considerable reliance is placed upon rectal examination to determine roughly the total bulk of tissue. The group of cases now considered suitable for transurethral resection constitutes roughly 95 per cent of the benign obstructive lesions encountered by the writer.

Where there are prostatic calculi the response to transurethral resection is particularly good. Occasionally the prostate gland will be reduced to a hollow sack filled with small calculi and upon the removal of the intraurethral portion of the gland the calculi may frequently be scooped out of the prostatic bed with the beak of the resectoscope. The remaining small portion of the obstructing gland is then trimmed off.

A good percentage of all obstructions at the bladder neck are complicated by the

* Read before the Section of Genito-Urinary Surgery, New York Academy of Medicine, December 16, 1936.

presence of bladder calculi. If the calculus and the obstructing gland are both small, the calculus may be crushed with the lithotrite and the obstructing tissue removed by the transurethral method. In dealing with this type of case I strongly advise dealing with the calculus first; otherwise it will interfere with the movement of the resectoscope during the operation. It may also interfere with the drainage of the indwelling catheter following operation, and after the catheter is removed, the calculus will have a tendency to fall into the funnel-shaped excavation at the bladder neck.

Stones over 3 cm. in size should be removed suprapubically, with transurethral resection after ten to fourteen days of suprapubic drainage. I do not believe small glands should be enucleated suprapubically simply because a suprapubic cystotomy wound is present. Transurethral operations under these circumstances may be done with practically no risk as compared with the mortality of suprapubic enucleation.

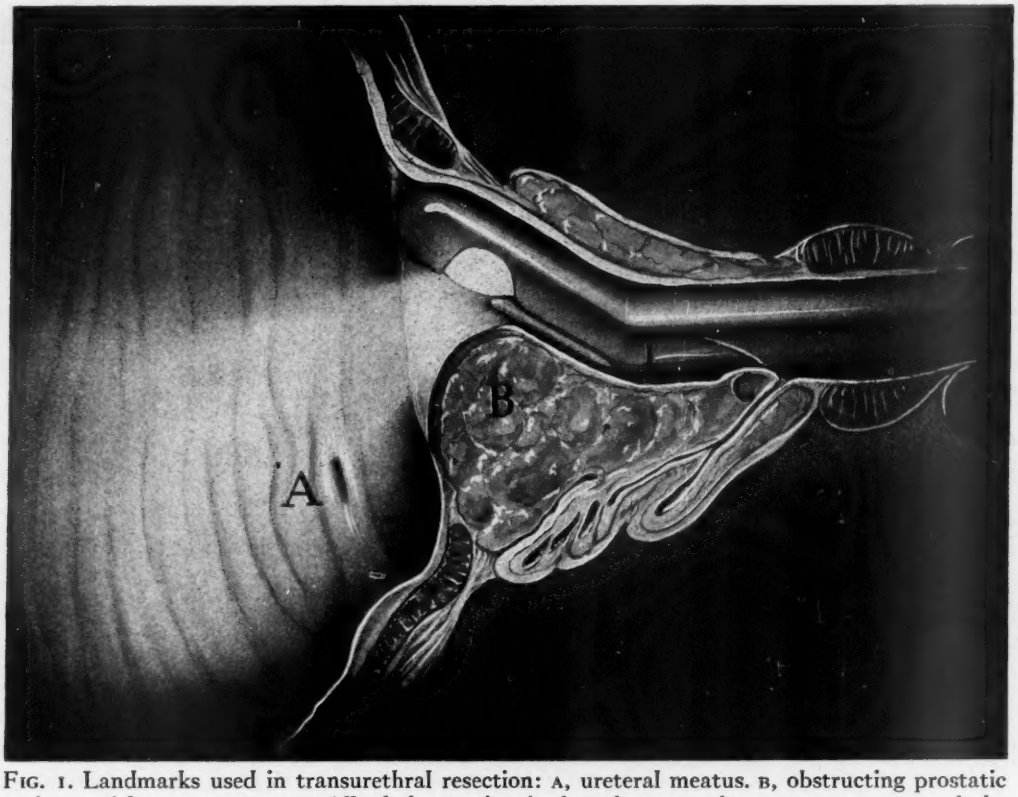

FIG. 1. Landmarks used in transurethral resection: A, ureteral meatus. B, obstructing prostatic tissue with verumontanum. All of the cutting is done between the verumontanum and the ureteral meatus.

The treatment of large diverticula of the bladder associated with an obstructive lesion at the bladder neck is a subject of controversy. The majority of these cases may be completely relieved clinically by the removal of the obstruction, although there is undoubtedly a certain number in which it is necessary to dissect out the diverticulum. Three cases of large diverticula have been treated by resecting the obstructing bladder neck, the capacity of the diverticula being respectively 8, 16, and 22 ounces. The first two patients mentioned emptied their bladders satisfactorily, with no residual urine, eight weeks after operation; the third patient has been observed for only twenty days postoperatively and the amount of residual urine varies from 2 to 4 ounces (as compared to 22 ounces

before operation). I know of no objection to trying transurethral relief of bladder neck obstruction in these cases with the idea in mind of resecting the diverticulum at a later date if necessary.

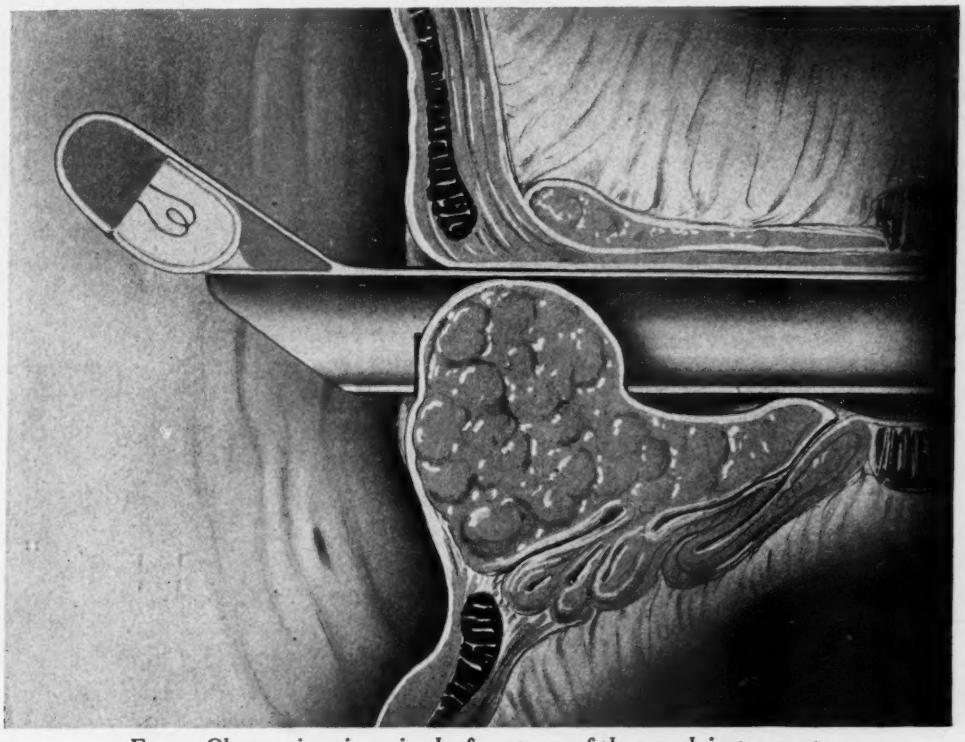

Fig. 2. Obstructing tissue in the fenestrum of the punch instrument.

In this series, the only female with bladder neck obstruction was a highly nervous spinster with an enormously hypertrophied internal sphincter. The imbalance between the neuromuscular apparatus had developed to such an extent that she had almost complete retention of urine for six days before operation. We realized we were treating effect rather than cause, but the distress was so great that it was decided to resect the internal sphincter, by removing one large bite from the midline. This has been followed by two years of relief.

Transurethral resection is attempted in all cases of carcinoma of the prostate. Resection of carcinomas for the relief of obstruction is, as a rule, very satisfactory. Some of the glands appear to be avascular and cut like cheese, and in these cases resection is quite easy and very satisfactory. However, the hard, scirrhous type of carcinoma is much more difficult and presents almost the same problem as the generalized fibrosis of the bladder neck. Whether or not the instrumentation stimulates metastases, I am not in a position to say, but the relief of obstruction in this hopeless condition is an important factor.

The presence of large amounts of residual urine should not deter one from transurethral resection. Acute retention may be caused by small glands and after adequate decompression these glands may be resected just as successfully as those with a small degree of retention. On the other hand, everyone has seen large glands producing relatively little obstruction. Relief of the symptoms of dysuria, frequency and nocturia may be the outstanding reasons for seeking relief; these are often as important an indication as large amounts of residual urine.

The above observations are based upon a consecutive series of 213 operations on 170 patients. About three-fourths of these operations were done with the Braasch-

Bumpus punch instrument. The last forty-two operations were done using the new Thompson "cold punch." This instrument has proved to be much more efficient than any used previously. The mortality rate has been particularly gratifying, only six deaths having occurred in the entire series. Three of the deaths occurred in malignant cases, leaving a mortality of less than 2 per cent in the benign group.

The last 101 consecutive cases have been operated upon without a fatality.

The clinical results have been very satisfactory. Postoperative complications and morbidity have been reduced to a minimum. Over one-half the patients were able to leave the hospital on the sixth postoperative day.

SUMMARY AND CONCLUSIONS

1. The selection of *cases* depends entirely on the operator's experience and ability. In the first fifty cases we should select only the easiest ones or those requiring the removal of the minimum amount of tissue.

2. Diverticula of the *bladder* will usually take care of themselves if the obstructing lesion is removed.

3. The cold punch operation has proved to be very satisfactory in almost all types of obstructive lesions. The results are good and the mortality is low.

In fractures of the distal end of the humerus integrity of circulation and nerves should be determined before reduction is undertaken.

PERSONAL EXPERIENCES WITH GAS BACILLUS INFECTION*

A REPORT OF FORTY-ONE CASES

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MANY men have contributed to our knowledge of gas bacillus infection. With the appearance of the "germ theory" of disease, organisms found associated with gas gangrene were investigated by such men as Pasteur, Novy, Koch, Welch and Weinberg. The clinical investigation of this disease has been described very well by such early workers as Stolz (1902), Cramp (1912), and Simonds (1915).

Interest was aroused in gas gangrene during the last great war and much literature was written about it. Possibly the best articles are the reports of the Surgeon General of the United States Army and the Great Britain Medical Council. Such investigation has provided a basic knowledge of the etiologic factors involved and pathologic changes which take place in the diseased tissues.

The extensive distribution of various gas-producing organisms is now generally recognized. Manson demonstrated that more than 34 per cent of chronic ulcers harbored gas bacilli. Roberts, Johnson and Buckner grew cultures of anaerobic spore-bearing bacilli from the unprepared abdominal wall skin of more than 21 per cent of persons examined. An abdominal wall gas gangrene resulted from diversified types of abdominal operations in twenty-one cases recorded by T. G. Orr. However, although the existence of these organisms is an accepted fact, results of treatment in the cases remain highly unsatisfactory. A mortality rate of 49.7 per cent was reported recently by Millar in an analysis of 607 collected cases of gas bacillus infection occurring in civil life. The American Expeditionary Forces in France reported a mortality rate of 48.152 per cent. These surveys are only unique in their vastness; the percentages quoted are borne out by countless similar reports.

Naturally the high mortality in these cases has caused many methods and combinations of methods to be utilized in treatment. The tragedy is that the acute necessity for this experimentation has caused it, to a certain extent, to defeat its own ends. So many methods of treatment are tried on the same gas infection case that estimating the value of each agent used becomes increasingly difficult.

J. F. Kelly recently studied the status of *x*-ray treatment in gas gangrene. He believes its use is valuable in both limb and trunk cases, and he begins treatment as soon as gangrene is suspected and continues it throughout the course, twice daily for at least three days. From his viewpoint, amputation seems detrimental, or at least unnecessary. He considers gas bacillus serum, local antiseptics, local minor surgery, and *x*-ray much safer, since all deaths in his series occurred in cases with amputation of an extremity, while all those having no amputation survived. Of the thirteen cases where amputation was utilized, five patients died and eight recovered, while of twenty-one with extremity involvement and no operation, none died. In two cases of this series no serum was used and both patients recovered, although one developed tetanus after the gangrene had subsided.

G. E. Konjetzny (Dortmund) observes that serum effect is difficult to estimate,

* Read before the Section of Industrial Medicine and Public Hygiene of the American Medical Association at Atlantic City, June 11, 1937.

and that some of the alleged benefit may be from the direct surgical treatment. However, after some personal experiences with these gas infections he believes serotherapy is effective.

The startlingly high mortality following treatment has inspired the suggestion of many procedures to cure this disease and consequently few conditions have aroused so much interest and so much controversial discussion. When that which is not established is done away with, the majority of the controversies simmer down to a few accepted points. The treatment of gas bacillus infection readily divides itself into two methods of therapy, prophylactic and active, both of which are preëminently operative. Early débridement and the use of delayed primary suture have brought the incidence of gas infection down to a low percentage.

TABLE 1
GAS BACILLUS INFECTION IN FORTY-ONE CASES

	Total Cases	Recoveries	Died
Surgery done for existing gas gangrene of an extremity.	1 débridement of arm. 3 amputation of arm. 3 amputation of legs. (2 legs on one patient) — 7	7	None
Amputation plus serum. Extremity cases.	6	5	1
Serum in septicemia. One case a gunshot wound; the other two cases contusions.	3	0	3
Serum plus incision of extremity. Septic cases.	5	1	4
X-ray treatment used in abdominal wall cases and where amputation seemed inadvisable.	14	4	10
Miscellaneous.....	6	4	2
Total cases.....	41	21	20

Active treatment of an existing gas bacillus infection has consisted of amputation, open incision, débridement, serum therapy and *x*-ray. The results of these methods of treatment or varying combinations of methods have been previously mentioned. That some of these methods have not been satisfactory and others have been, according to the literature reviewed, is most interesting. We wish to present our own personal cases and the mortality resulting in the various methods of treatment used. An analysis is summarized in Table 1.

The following cases were seen and treated by the Junior author, on the *x*-ray Service of Dr. C. H. Warfield at the Cook County Hospital, and from the Surgical Service of Dr. E. P. Coleman, Canton, Illinois, since the World War.

CASES REPORTED

In the first group of cases, nothing in the way of treatment was done for the patient except surgery. Gas infection was present in an extremity in all seven cases. Clinically, these cases were those of gas gangrene of an extremity from twenty-four to ninety-six hours in duration. Five of the cases were cultured and Bacillus welchii was discovered. Immediate amputation was performed and no persons died. One of these patients had gas gangrene of both legs. Both legs were amputated and the patient recovered.

Six cases of existing gas infection received serotherapy in addition to surgery (amputation). Only one death occurred, and we believe this man had gone too long for help, since an extensive infection and septicemia had developed. All six cases were clinically and bacteriologically gas bacillus infections.

Serotherapy alone was unsuccessfully used in three cases of gas bacillus septicemia, all of which proved fatal. One case was the result of a gunshot wound of the abdomen; the other two followed extensive lacerations of extremities. Post-mortem examination showed that all the patients died of septicemia resulting from gas bacillus infection.

In five cases diagnosed as septicemia, serotherapy was used, plus extensive débridement of the extremity, but only one patient recovered. That case was probably not one of septicemia. Recovery occurred with late amputation (seventh day).

X-ray treatment was used alone in fourteen cases, resulting in four recoveries and ten deaths. Three developed gas bacillus infection of the abdominal wall following operation and were lost. Postmortem examination showed that these patients died of gas bacillus septicemia. One developed gas gangrene postoperatively, following a gunshot wound of the abdomen. *X*-ray was tried, but again to no avail. Autopsy showed a generalized gas bacillus septicemia. Ten of the patients had a far-advanced gas bacillus infection of an extremity. Amputation seemed inadvisable at the time and *x*-ray was tried alone. Six died of septicemia. Four of these six were brought to autopsy and showed gas bacillus septicemia as the cause of death. In the four cases that responded to *x*-ray, wide opening and amputation resulted in recovery.

Two deaths resulted in six cases which received varied combinations of treatment. One patient had a gunshot wound of the abdomen, with seventeen perforations of the ileum. After operation and repair, he was given serotherapy, but died of generalized septicemia of gas bacillus type, as shown at autopsy. There was no peritonitis present. In another case, a gunshot wound of the thigh developed gas gangrene. *X*-ray, débridement, and serotherapy were tried but the patient died of a gas bacillus sepsis. One man developed gas bacillus infection of low virulence in a clean amputated stump, after amputation had been performed for diabetic and arteriosclerotic gangrene. The amputated stump was laid wide open and the patient was given serotherapy, with recovery. Later, a secondary amputation was necessary. Three of this group had gas gangrene of an extremity from gunshot wounds. Amputation and serum were used, but gangrene developed in the amputated stump, requiring a secondary amputation, after which recovery took place.

DISCUSSION

Considering the cases as a whole, we find a mortality of 48.7 per cent. These cases were taken as they came, and usually were seen in a well advanced or very late stage of the disease.

When further analysis of the individual deaths was completed, autopsy showed that these deaths were due to gas bacillus septicemia. Our results coincide with those of others in disclosing that acute gas bacillus infection may rapidly become a generalized septicemia.

In local forms of gas infection progress of extension is not by the blood or lymph stream, but by direct development through the muscle and fascia involved. Such local types may get into the blood stream and cause a septicemia. Consequently, the prophylactic treatment of these gunshot wounds and acute traumatic cases is complete débridement. If the gas infection is local and in a local muscle group, probably open incision and excision are enough for cure. In the advanced case, as most of these were, amputation, we believe, is a life-saving measure if septicemia has not set in. Amputations are not always successful because the gas infection has already become a septicemia. We believe that promptness of diagnosis and the institution of early amputation are the factors of prime importance if this condition is to be averted.

Dr. George Davis first demonstrated the importance of early recognition of gas infections by use of *x*-ray findings (1916), and we find this a great help in early diagnosis as well as assisting in determining early treatment. We find that in the cases we have to report, when amputation is performed and a septicemia is already present, the infection travels rapidly to a fatal termination without any benefit from removal of the original source of infection.

CONCLUSIONS

We believe that in handling gas bacillus infections no single remedial agent should be solely relied upon. Polyvalent serotherapy may be of value when associated with active surgery, but considering the great number of strains of anaerobic organisms, as shown by Weinberg, it is doubtful whether serotherapy would meet all contingencies. We believe that early recognition and immediate treatment of gas bacillus infections are absolutely essential and that *x*-ray findings may be of great aid in expediting diagnosis of gas infection.

This group of cases is, of course, too small to let us draw definite conclusions, but we fail to see any help for these individuals through early diagnosis and proper surgery. The added influence of serotherapy and *x*-ray therapy may also be used, but we believe they are not determining factors unless proper surgery has been done early in the progress of the disease. *X*-ray therapy alone was disappointing and failed to give the results we had been led to expect.

REFERENCES

Cramp. *Ann. Surg.*, 56: 544, 1912.

Kelly, J. F. *X*-ray in gas gangrene. *Radiology*, 26: 41–44 (Jan.) 1936.

Koch. *Mitt. a. d. Kaiserl. Gesundheitsamte*, 1: 1, 1881.

Konjetzny, G. E. *Klin. Wchnschr.*, 13: 831 (June 9) 1934.

Manson. Pathologic gas producing anaerobic bacilli in chronic ulcers. *Arch. Surg.*, 24. 752 (May) 1932.

Millar. Gas gangrene in civil life. *Surg., Gynec. & Obst.*, 54: 232 (Feb.) 1932.

Novy. *Ztschr. f. Hyg. U. Infektionskrankh.*, 58: 209, 1894.

Orr, T. G. Gas bacillus infection following clean amputations. *Am. J. Surg.*, 25: 113 (July) 1934.

Pasteur. *Bull. Acad. d. méd. de Paris*, 11: 781, 1877.

Report of Medical Research Committee. Series No. 39. Anaerobic Infection of Wounds. London 1919.

Reports to the Surgeon General (U. S. Med. Corps). Vol. 12, p. 407.

Roberts, Johnson, and Bruckner. The aseptic peritoneal cavity—a misnomer. *Surg., Gynec. & Obst.*, 57: 752 (Dec.) 1933.

Simonds. *München. med. Wchnschr.*, May, 1915.

Stolz. *Beitr. z. klin. Chir.*, 33: 72, 1902.

Weinberg and Francon. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 43: 1084, 1919.

Welch. *Bull. John Hopkins Hosp.*, 11: 185, 1900.

FURTHER STUDIES ON THE INTRAPERITONEAL USE OF BOVINE AMNIOTIC FLUID IN ABDOMINAL SURGERY*

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THE intraperitoneal administration of bovine amniotic fluid at the time of operation has held our attention for the past five years. We have employed it chiefly in the hope that we might be able to promote a smoother postoperative convalescence, eliminating or at least ameliorating some of the factors, such as nausea, gas pains, and distention, which prove so annoying to the patient. This course was suggested by Johnson's observation[1] that the agent under consideration decreased distention, shortened the period of emesis, and hastened resolution when used in experimental animals.

In a previous report[2] published in 1935, we felt that enough proof of its beneficial effects had been adduced to justify a second series of cases.

As in the previous study, this work has been carried out on the Gynecologic Service of the Third (New York University) Surgical Division of Bellevue Hospital. The agent used was a concentrated sterile fraction of bovine amniotic fluid, known as amfetin. The technique of administration was described previously.[2] It consisted essentially of introducing 400 c.c. of previously warmed amfetin into the abdomen just before tying the final peritoneal suture.

Preceding the administration of amfetin to any of our patients, we employed it in a number of experimental animals that had been subjected to various forms of severe peritoneal trauma and irritation such as might be encountered or produced during major surgical procedures. A similar group of animals was subjected to the same operative procedure, but had normal saline administered intraperitoneally. Both groups of animals were reoperated on several times at intervals of three weeks and all finds were carefully noted. Briefly, the results were as follows:

1. Both groups of animals showed adhesions three weeks after the initial operation, but the animals treated with amfetin showed fewer adhesions, which were less dense and easier to separate. This coincided with the results of a previous study made by Lacey.[3]

2. Repeated separation of adhesions at subsequent operation resulted in more numerous and denser adhesions in the group of cases receiving saline, while the group receiving amfetin showed fewer and thinner adhesions.

3. The animals receiving amfetin survived twice as many operative procedures as the group in which saline was used.

4. The amfetin group presented a better postoperative appearance, retained fluid and solid food earlier, and was more active than the controls.

With these observations in mind, we set about outlining a possible course of study on the human. Bearing in mind the infrequency of reoperation on this service, with the resultant paucity of information as to the effects of any agent in modifying the formation of adhesions, we undertook the clinical study of amfetin as related to postoperative convalescence.

Out of 100 consecutive patients having a celiotomy, the fifty presenting the most marked pelvic pathology at the time of operation were given amfetin, and the remaining fifty were used as controls.

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It was found in this first study that of the amfetin group, 74 per cent of the patients had dense adhesions at the time of operation, while 10 per cent of the control group were similarly complicated. The postoperative results were encouraging, in that nausea, vomiting, distention and gas pains seem definitely to be decreased by the use of amfetin. This was in accord with the findings of Trusler,[4] who states that "these patients tend to enjoy a smooth postoperative course."

In addition to these and other measured findings, there were several subjective factors which were rather elusive when the time came to evaluate them. For example, it was thought that a patient who had received amfetin at the time of operation subsequently had a softer abdomen, expressed a desire for food earlier, and as a rule was brighter than a similar control patient. It was also thought that most of the amfetin patients more nearly approximated normal posture when allowed out of bed. However, it should be borne in mind that these are impressions only, and not definite findings.

TABLE I
OPERATIVE DIAGNOSIS

	Control	Amfetin
Fibroids	24	30
Fibroids with adnexal disease	9	7
Adnexal disease	32	28
Retroversion	24	15
Ovarian cyst	13	9
Endometriosis	0	1
Fundal malignancy	0	1
Ectopic pregnancy	14	4
Appendicitis	0	1
Perforation of uterus	2	0
Intrauterine pregnancy	7	4
	125	100

With these facts as a background, the present study was undertaken in an effort to substantiate or modify our previous conclusions. Different standards were adopted which tended to emphasize those factors which we were most desirous of determining.

The cases treated with amfetin in this second series were, as a rule, not selected, but taken more or less alternately with the control cases. It must be added, however, that if a particularly difficult case was encountered, that patient usually received amfetin. Control patients numbered 125, while 102 received amfetin, making a total of 227 patients observed.

The surgeons, anesthetists, and operating room technique were essentially similar in both groups. The anesthetic agents were nitrous oxide and ether.

With the exception of one case of lobar pneumonia in each group, there were no major complications. Wound infections were equal in each group.

Tables I to VII summarize the other results. In Table I are listed the operative diagnoses in the last two groups. There is a preponderance of ectopics in the control group, and of fibromyomata in the amfetin group. Otherwise there is no marked difference in the two categories of patients.

TABLE II
OPERATIVE PROCEDURES

	Control	Amfetin
Complete hysterectomy with salpingo-oöphorectomy	1	1
Supracervical hysterectomy	16	16
Supracervical hysterectomy with salpingo-oöphorectomy	20	29
Salpingo-oöphorectomy	33	21
Salpingectomy	11	8
Tubal plastic operations	3	3
Suspension of uterus	15	7
Suspension of uterus and adnexa	12	8
Myomectomy	1	4
Hysterotomy	7	4
Repair of perforated uterus	2	0
Appendectomy	0	1
Little's operation	4	0
	125	102

In Table II are listed the major or most important operative procedures performed in each case. Here again there is no marked difference, except in the number of uterine

suspensions performed on the control patients, and the slightly greater number of hysterectomies performed on the amfetin patients.

Table III
ADHESIONS

	Control, Per Cent	Amfetin, Per Cent
Adhesions present	39.70	53.84
Adhesions absent	60.30	46.16
Dense adhesions	13.6	20.6

In Table III it will be noted that approximately 40 per cent of the control group were found to have adhesions at the time of operation, whereas 54 per cent of the amfetin group were similarly affected. Also, it will be noticed that dense adhesions, of a fibrous type, were present in 13.6 per cent of the controls, and 20.6 per cent of the amfetin patients. This would seem to indicate that the group of patients treated with amfetin presented slightly greater possibilities for a disturbed postoperative course than the control group. This difference was present in spite of an effort to use this substance on alternate cases.

It might be well to add here that the filmy, easily separated type of adhesion is not included in these statistics. The incidence of dense adhesions seems high in both groups, since these patients were studied at Bellevue Hospital, where the result of extensive pelvic inflammation is commonly encountered.

In Table IV we have the average daily measurements of the abdominal circumference at the level of the umbilicus, these measurements being taken immediately postoperatively, and on the afternoons of the first, second, third and fourth postoperative days. Analysis of these figures shows 21 per cent more distention, as measured in inches, in the untreated or control group. Actually, as can be seen from the figures, this difference represents only a small increase of distention in the control group.

Table IV
AVERAGE ABDOMINAL MEASUREMENTS (DISTENTION)

	Control, Inches	Amfetin, Inches
Immediately post-operative	29.59	29.31
24 hours post-operative	30.50	30.07
48 hours post-operative	30.91	30.58
72 hours post-operative	30.78	30.35
96 hours post-operative	30.64	30.17
VOMITING		
Number of attacks first 24 hours (average)	1.5	1.25
Number of attacks after 24 hours (average)	1.43	.73

The second part of the table shows the average number of times patients in each group vomited during the first twenty-four hours, and also during the subsequent ninety-six hours. During the first twenty-four hours the amfetin patients enjoyed a 17 per cent advantage. During the subsequent ninety-six hours, the amfetin patients vomited only half as many times as did the control patients. It is interesting to note in this connection that Lacey,[5] in a similar study, found that the duration of vomiting in the amfetin group was 11.84 hours, while in the controls it was prolonged to 18.14 hours. He also found that when spinal anesthesia was employed, the amfetin group averaged vomiting 1.25 hours, while the controls extended this period to 19.14 hours. This forces one to wonder if most of the nausea and vomiting found in the amfetin group of the present study is not due to the effects of the anesthetic employed.

The results in Table V are not so encouraging, for while the amfetin group shows a slight advantage in the number of patients who suffered no gas pains, the severe seizures were more numerous in the amfetin group. This is contrary to our findings in the first series of patients studied. Likewise, the moderately severe attacks in the amfetin group, while less numerous than in the controls, are still

TABLE V

	Control, Per Cent	Amfetin, Per Cent
Gas Pains		
Slight	27	29
Moderate	44	33.5
Severe	7	7.5
No pains	22	30.0
Nausea		
Slight	24.5	31.7
Moderate	31.7	22.1
Severe	9.6	6.7
None	34.2	39.5

much more frequent than in our first series of cases. The second part of the table shows some advantage for the amfetin patients as far as nausea is concerned, but again there is a discrepancy between the figures in this series and our first one. The increase in the slight columns has been referred to before in discussing our theory of shifting as a result of modification of the usual reaction.

TABLE VI

	Control	Amfetin
Average highest pulse rates		
First 24 hours	109	109
Second 24 hours	109	107
Third 24 hours	102	103
Fourth 24 hours	96	95
Average of highest temperatures		
First 24 hours	100.7°F.	100.7°F.
Second 24 hours	100.7°F.	100.6°F.
Third 24 hours	100.2°F.	100.2°F.
Fourth 24 hours	99.6°F.	99.7°F.

Table VI summarizes the average temperature and pulse rates for the two groups. The similarity of the figures precludes any suggestion of a beneficial or deleterious effect on these factors.

We also find a striking similarity in the pre- and postoperative blood pressures of both groups. The average duration of anesthesia and the average operating time is slightly longer in the amfetin group. The average number of catheterizations in the control group exceeded those of the amfetin group by 22 per cent. Also it will be noticed that the amfetin patients began voiding about six hours earlier postoperatively than did the control patients. Peristaltic sounds were heard seven hours sooner in the average amfetin patient than in the average control.

TABLE VII

	Control	Amfetin
Blood pressure (average)		
Preoperatively	119/76	122/79
Postoperatively	118/75	121/77
Time anesthetized (average)	64.75 minutes	68.33 minutes
Operating time (average)	55 minutes	59.6 minutes
Average number of catheterizations per patient	1.81	1.41
Average number of hours before voiding post operative	24.70 hours	18.71 hours
Average number of hours before peristaltic sounds were heard	46	39.3

SUMMARY

1. One hundred and two patients received 400 c.c. of amfetin each at the conclusion of gynecologic celiotomies, the agent being introduced into the peritoneal cavity.

2. One hundred and twenty-five patients having similar operations under similar conditions, but not having amfetin administered, were used as controls.

3. The postoperative clinical condition and reaction of patients was closely observed and, where possible, these factors were measured in terms of known units.

CONCLUSIONS

1. The intraperitoneal administration of a concentrated sterile fraction of bovine amniotic fluid at the time of operation has no appreciable effect on blood pressure, pulse, temperature or number of wound infections.

2. The effect on postoperative adhesions in the human is not known to the authors,

none of our 227 cases having come to reoperation.

3. Normal intestinal motility and normal contraction of the bladder seem to return to normal sooner when amfetin is administered.

4. The intraperitoneal use of amfetin at the time of operation holds definite promise of affording the patient varying degrees of relief from nausea, vomiting, gas pains and distention.

REFERENCES

1. Johnson, Herbert L. *New England J. Med.*, 199: 661 (Oct.) 1928.
2. Gepfert, J. Randolph. *Am. J. Surg.*, 32: 40 (April) 1936.
3. Lacey, James T. *Ann. Surg.*, 92: 281, 1930.
4. Trusler, H. M. *Arch. Surg.*, 22: 983 (June) 1931.
5. Lacey, James T. *Ann. Surg.*, 101: 529, 1935.

Supracondylar fractures of the flexion type are infrequent. They usually require open reduction.

IMPORTANT RECKONINGS IN BILIARY SURGERY*

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IN spite of the progress made in the management of biliary disease, there are so many patients who are not relieved of their difficulties after they once have submitted to treatment, that what confidence once rested in the attending physician is lost, and the difficulties of the problem are magnified. There is very little to be gained in the study of good results, but an honest and painstaking investigation of poor results obtained may lessen their incidence and otherwise convert them to satisfactory ones.

The greater contributions to surgical advance in recent years have apparently come by way of the biochemical and physiologic laboratories rather than by way of the operating room. It is not intended that this paper shall be all inclusive; a great many interesting features concerning problems associated with biliary surgery have been excluded from this discussion.

In a five-year study of 249 biliary cases in a well rated private institution, there were:

	No. of Cases	Deaths	Per Cent Mortality
Acute cholecystitis	63	11	16
Chronic cholecystitis	127	16	12½
Cholelithiasis	59	6	10.1
	249	33	13.2

This could reasonably be taken as an index of what is actually accomplished by present preoperative and operative routine, but these figures seem altogether too high. A further review of postoperative morbidity would also show some astoundingly poor clinical results with treatment by present methods.

The results on the average service, in the average municipal hospital, are better by far than those of private institutions, because charity patients may be kept in the hospital preoperatively, careful laboratory determinations are not wanting and medical coöperation is always available without cramping the surgeon's freedom in preoperative study.

While some clinics report very inspiring results in the management of biliary disease, the profession as a whole has no cause to rejoice over the results now obtained. The bulk of surgery is not being done under conditions that obtain in better clinics. In spite of repeated pleas for lessening the mortality and morbidity in the treatment of diseases of the gallbladder and bile ducts, too small a number of converts have been made to this cause.

Poor results may be enumerated briefly as:

1. The fatal termination of a case.
2. Recurrence of symptoms which antedated treatment and which offered the chief indication for treatment.
3. Recurrence of pathology which the treatment instituted was intended to eliminate: bile stasis, biliary dyskinesia, common duct obstruction and intrahepatic calculi.
4. The occurrence of an aftermath more disturbing to the patient than the symptom complex for which originally the patient sought relief, such as inadequately treated hepatitis associated with duodenal stasis due to functional disease of reflex origin, or obstructive from adhesions.

The basic causes of death are practically the same, whether patients die following appendicitis, pneumonia, compound frac-

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tures, or stone in the common duct. Death is determined by the product of the damage done by preëxisting disease, the seriousness of the pathologic process encountered, the untoward effect of the treatment instituted, and lastly, failure to supplement the operative element of treatment with other measures which may and often will turn the tide of defeat. While surgery is an important factor in determining the outcome in a given case, it is far indeed from being the major element. The damage done by preëxisting disease may be totally beyond the scope of treatment, but the changes suffered by the heart, liver and kidneys, as well as the altered metabolism and body chemistry, must be reckoned with. These changes must strongly influence the plan of attack, whether the lesion is in the gall-bladder or common duct. This calls for scrupulous preparation of the patient for the ritual of the operating room.

Heart. Too often an examination of the heart consists in listening to the heart sounds, the recognition of murmurs if present, and a notation of the pulse rate. Some include an electrocardiogram, which does not invariably point out existing disease, while others place considerable reliance on the circulation time. Cardiac efficiency cannot, however, be estimated with the patient lying in bed. It is true many patients are unfit to be put through a test of cardiac action under effort, but those who can should certainly be checked to determine what the heart may do upon exertion. A surgical procedure, particularly in the upper abdomen, is often found to be an imposition too severe to be borne.

In biliary cases, in which demonstrable cardiac pathology is so often concurrent, it is important to determine the best procedure to lessen the risk as far as the management of the heart is concerned. Shall the patient be digitalized before or after operation? Is bed rest adequate preparation for upper abdominal operations, and what cardiac stimulation is of value if stimulation becomes necessary? If these questions were settled in our minds a good step in the proper direction might have been taken. Certainly regardless of how we feel about these questions, the prime issue remains the accurate evaluation of cardiac efficiency as a factor in determining the limitations to be set for any surgical procedure undertaken.

The most valuable method of determining cardiac efficiency is by measuring the vital capacity. This factor is the truest criterion of myocardial function. It is lowered by (1) myocardial damage; (2) diminution in elasticity of lung parenchyma; (3) the presence of cardiac hypertrophy; (4) pericardial or pleural effusion encroaching upon the volume of the thoracic cage; (5) mediastinal lesions producing cardiac embarrassment; and (6) limitations of diaphragmatic excusion by subdiaphragmatic lesions producing pain or pressure.

Churchill and McNeill[1] state that "if it is realized that an operation involving the muscles of the abdominal wall temporarily leaves the patient with but 25 to 50 per cent of his preoperative vital capacity, it is readily understandable that a patient with an initial reading which approaches the tidal air requirement will be subjected to a grave risk by such a procedure."

Many prolonged procedures are done under unwisely chosen anesthesia, in inadequately and poorly equipped patients, who most likely would have survived had less surgery been done, or had regional or local anesthesia been employed. In chosen cases, survival is possible if the patient is given some opportunity and time to prepare the heart for the coming crisis.

Kidneys. Death of a patient on the fourth or fifth day after surgery is more often due to renal shutdown than to infection, especially in patients falling in the age groups of biliary disease subjects. One must shudder at the thought that in this day and age patients are still submitted to major surgical procedures with a urine analysis as the only index of kidney

function! Here again the surgeon is still too ready to ignore the value of the aid obtainable from a coöperating internist. Not enough preliminary estimations of the functional capacity of the kidneys are made. Thus, when considering blood chemistry preliminary to surgery, we are inclined to feel assured of a fair kidney function when we find urea nitrogen figures within what are called normal limits. A low blood urea, instead of indicating good elimination via the kidney, may point to a severe breakdown in liver function, since urea is synthesized in the liver. A low figure for blood urea can be of value only after the functional efficiency of the liver has been established in deamidizing proteins brought there from the intestinal tract via the portal vein.

Liver. In order to appreciate the relative importance of changes occurring in the liver, one must be acquainted with the functions now associated with that organ. One often hears that very little is known concerning the physiology of the liver. If, however, what is known about the liver were common knowledge, it would inevitably lead to a better understanding of the problems involved in the management of the pathologic states encountered. The term hepatitis means very little in terms of disturbed physiology, since a healthy looking liver at operation may be a very poorly functioning one, and vice versa.

In appraising the assets of a patient prior to surgical intervention, it may be very important to know certain facts about the functional status of the liver, e.g.: What is the capacity of the liver with regard to the regulation on the blood sugar level? Opie and Alford,[2] after extensive experimentation, have concluded that diet exerts a profound influence on the toxicity of certain substances which cause parenchymatous cell necrosis in liver and kidney. They have shown that susceptibility to liver and renal poisons is less after a diet rich in carbohydrates. Our gall-bladder patient can therefore be greatly aided by preoperative saturation of his liver with glycogen. Insulin need not be used with intravenous glucose, since there is no evidence that insulin enhances the glycogen storage in the liver. Ravdin[3] gives all his liver cases 14 per cent of the total caloric requirements as proteins prior to operation in order to reduce the liver fat.

Following hepatectomy in dogs there is a progressive fall in the blood sugar level and the typical picture of increasing hypoglycemia develops. Coma and death follow. Intravenous glucose restores the sugar level and the normal appearance of the animal, but this restorative measure is of no value in previously pancreatectomized animals. Bollman, Mann and Magath[4] have pointed out that although the total amount of glycogen in the muscles is as great as, or greater than, that in the liver, muscle glycogen plays a very minor part in the regulation of the blood sugar. The dehepatized animal does not liberate muscle glycogen fast enough to prevent the early development of hypoglycemia. The glycogen storage in the muscles apparently is mainly reserved for muscular activity and the supply of sugar to the blood is almost entirely dependent on the functioning of the liver.

If the kidneys are removed at the same time as the liver, the blood urea remains constant at the level before operation, but amino acids accumulate in the blood, urine and tissues following hepatectomy. When amino acids are given intravenously or orally there is a rise of these substances in the blood and urine, but the values for urea remain unchanged. Uric acid also increases in the blood following hepatectomy. Hence the liver is necessary for the deamidization of amino acids, the synthesis of urea and the phases of destruction of uric acid in the metabolism of proteins and urea.

The liver also bears an important relation to the metabolism of the constituents of bile. Mann, Sheard and Bollman[5] have shown that bilirubinemia and bilirubinuria follow hepatectomy in dogs within three hours and that jaundice increases progres-

sively until the animals die. Using photospectroscopic methods, Mann and his associates found the pigment responsible for this jaundice was identical with bilirubin and that it is formed principally in the bone marrow and to a lesser extent in the spleen and the liver. In this respect therefore the liver is an excretory organ.

Human blood fibrinogen normally amounts to 0.27 Gm. per 100 c.c. of blood. It is markedly reduced in animals by liver damage, occlusion of hepatic vessels after hepatectomy and in cases of liver lesions produced by phosphorus poisoning and acute yellow atrophy.[6] Complete knowledge concerning the bleeding tendency of jaundiced patients is, however, still wanting. The maintainance of blood fibrinogen level by the liver has been studied by many investigators and it is generally agreed by them that the degree of liver damage necessary to produce a fall in the fibrinogen level is considerably greater than that met in simple obstructive jaundice.

Ravdin, Riegel and Morrison[7] feel that the hemorrhagic tendency of the patient or animal suffering from an obstruction of the common bile duct is not due to a deficiency of any known substance in the blood which normally takes part in the clotting mechanism. At present the general belief is that neither the bleeding time, the coagulation time, the blood calcium nor the fibrinogen content in the circulating blood offers any criterion for defining the bleeding tendency in jaundiced patients. Only one thing is true: that at present, with the exception of blood transfusion, carbohydrates by mouth or intravenously offer the best hope of preventing hemorrhage in patients with obstructive jaundice.

Since any or all the liver functions may be impaired to a degree, the appreciation of what is known to be going on will eliminate the element of surprise at postoperative complications. When disturbed function has been recognized, and as far as possible improved in the preoperative period, the surgeon is prepared for eventualities.

Many tests have been elaborated to help chart the assets of the patient about to be subjected to biliary surgery. Some of these tests are more valuable than others. The coagulation time, bleeding time and icterus index are of value only for determining the effectiveness of preoperative treatment. They require no amplification here.

The test of dye retention of Rowntree and Rosenthal is based on the knowledge that phenoltetrachlorphthalein is excreted solely by the liver, the disappearance of the dye from the blood being determined colorimetrically. Hence there is justification in guarding from surgery patients who fail to show a dye excretion incompatible with the risk of the operation planned.

The galactose tolerance test is of considerable value in determining the degree of liver damage. The interpretation given to it is applicable in cases where frequent blood chemistry determinations are not readily available. It has been pointed out that the elimination of 5 Gm. of reducing substance within five hours following the ingestion of the galactose very often is associated with an early death from hepatic insufficiency.

Operation. The operative technique in biliary surgery is perhaps the least determining factor. Everything else being equal, the writer is convinced that it matters little which of the various operative procedures are instituted as far as the ultimate result in a given case is concerned. Every surgeon will employ the procedure best suited in a given case after he has identified the nature and extent of the existing pathology.

Nevertheless, the ungratifying results of treatment both as regards mortality and morbidity, our failure to lower the death rate, as shown by figures for the United States Registration area, and our probable failure in checking the morbidity incidence, show that the immediate and remote results in biliary surgery are not too dependent upon the type of surgery done. Surgeons who are too pleased with their

results are very likely not following their patients long enough.

The problem of the stoneless gall-bladder is still begging for clarification. Since the gall-bladder is merely a diverticulum of a very extensive system of ducts, it appears that the patient in whom this organ is not functioning, should not be a candidate for its removal. Its lost function indicates that the patient has cholecystectomized himself. Why not consider that the body has thus cholecystectomized itself in self-defense, and eliminate the risk of death now too often following surgical cholecystectomy? The unwisdom of cholecystectomy in such cases is seen in the frequency of distressing functional disorders which follow the removal of a stoneless gall-bladder. This does not mean, however, that a gall-bladder which is a part of pathology in the right upper quadrant, and which produces tugging or other defects in the smooth function of the pylorus or duodenum, should be allowed to continue producing such disturbance.

In line with recently accumulated experimental and clinical data, it would appear that such cases of stoneless cholecystitis should not be subjected to cholecystectomy. These patients are suffering from hepatitis and pancreatitis, not from anything that results from the functionless gall-bladder. They should be treated medically by means of small frequent feedings of protein (preferably meats), fats and carbohydrates. The presence of food in the stomach and duodenum relaxes the sphincter of Oddi, thereby decompressing the extrahepatic ductal system. Meat has a great tendency also to rehabilitate the liver afflicted with chronic fatty infiltration, so prominent a feature in all biliary pathology. The fat in the diet, while it may in some cases produce symptoms of intolerance, is still necessary, inasmuch as it stimulates the flow of bile. Its stimulative action is less than that of meat, and it may be given in doses just short of producing the symptoms of fat intolerance. The administration of carbohydrates requires no further recommendation.

Cholecystograms. Since many conditions other than those which have their seat in the gall-bladder may be responsible for an *x*-ray diagnosis of a non-functioning gall-bladder, such a diagnosis must be interpreted in the line of newer knowledge. It has been shown that 40 per cent of all roentgenologically pathologic gall-bladders can, under treatment, be rendered roentgenologically functional. The value of *x*-ray diagnosis is subject to considerable limitations throughout. Yet is there any surgeon who has not operated upon a gall-bladder wherein he was tempted to interfere surgically, primarily because of the *x*-ray report? It seems that at present a fair evaluation of cholecystography must include an appreciation of its limitations and as a result its greatest value must lie in those cases where the roentgenologist finds biliary calculi.

CONCLUSIONS

Pre- and postoperative treatment is most effective in determining the results in any given case of biliary disease.

Liver pathology, inadequately appreciated before or at the time of operation, is largely responsible for unfavorable results.

Cholecystectomy, so far, is the better procedure in calculous cholecystitis.

Cholecystostomy, followed by a long drainage (eight to twelve weeks), will greatly lessen the unfavorable aftermath in cases of non-calculous cholecystitis associated with a definite hepatitis.

A number of patients who have undergone surgery for stone and who have had a scrupulous investigation of the common and extrahepatic ducts, will occasionally return with more stones; it must be concluded that stones in some cases at least, may form in the extrahepatic ducts rather than in the gall bladder.

Morphine administered to patients suffering from biliary colic is dangerous. While acting on the sensory cortex in the brain, it is nevertheless responsible for the production of a spasm of the sphincter of Oddi. This produces an increase of pressure in the extrahepatic ducts from a normal or

0–30 mm. of water to 300 mm. of water (McGowan, Butsch and Walters[8]). This is far above the capillary pressure—hence the damage to the liver lobule. Instead of morphine, nitroglycerine and erythrol tetranitrate have been employed by the writer with very gratifying results.

Once a diagnosis of biliary pathology is made, it is the surgeon's duty to have the patient's physiochemical assets in the best possible condition before undertaking operative procedures.

So far, the advocates of cholecystectomy for the acute gall-bladder have not proved their case. While some clinics report a low mortality in these cases, one shrinks from the fear that the practice might become generalized. Cholecystostomy in such cases is still a safer procedure, carrying with it a minimum of risk. It is becoming a greater favorite with many. Unfortunately the rank and file who practice cholecystectomy for acute cholecystitis do not oblige by publishing their figures, and from the observation of the writer there are extremely few clinics that can show a lower than 10 to 20 per cent mortality for the cases in question.

Employing physiologic and chemical data, the surgeon has a more thoroughly equipped armamentarium for the better management of biliary cases.

REFERENCES

1. Churchill, E. D., and McNeill, D. Reduction in vital capacity following operation. *Surg., Gynec. & Obst.*, 44: 483 (April) 1927.
2. Opie, E. L., and Alford, L. B. Influence of diet upon necrosis caused by hepatic and renal lesions. *J. Exper. Med.*, 21: 1–37, 1915.
3. Ravdin, I. S. Personal communication.
4. Bollman, J. L., Mann, F. C., and Magath, T. B. *Am. J. Physiol.*, 74: 238, 1925.
5. Mann, F. C., Sheard, C., and Bollman, J. L. Studies of the physiology of the liver. XI. The extrahepatic formation of bilirubin. *Am. J. Physiol.*, 74: 49–60, 1925.
6. Best, C. H., and Taylor, N. B. The Physiological Basis of Medical Practice. Baltimore, 1937. Wm. Wood & Co., Chapt. 1, p. 7.
7. Ravdin, I. S., Riegel, C., and Morrison, P. J. Haemorrhagic tendency in obstructive jaundice. *Ann. Surg.*, 101: 605–611, 1935.
8. McGowan, J. M., Butsch, W. L., and Walters, W. Pressure in the bile duct of man. Its relation to pain following cholecystectomy. *J. A. M. A.*, 106: 2227–2230, 1936.

MANAGEMENT OF THE DESPERATE APPENDICITIS CASE*

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IF we are unreservedly to believe the statistics on appendicitis mortality we find that there has been a decided increase during the last thirty years. However, the statistics seem to be wholly unreliable because deaths due to appendicitis were formerly often not reported as such, but simply as peritonitis or intestinal obstruction. This is now no longer the case; the original appendicitis, listed as the cause of death, brings about an apparent increase in frequency.

The changing mode of living shows a definite tendency to increase the appendicitis incidence. A thorough statistical survey conducted in Germany covering the years of 1910 to 1929 shows that in a population of approximately 63,000,000 in 1910 there were 3,826 deaths from appendicitis in 48,996 cases. During the years of the war there was a gradual decrease of appendicitis deaths as well as a decrease in the number of appendicitis cases diagnosed. This was ascribed to more restricted diet and a more simple mode of living. By 1929 when the population of Germany was the same as in 1910 the deaths from appendicitis were 5,721 in 210,512 cases. The statistics also cover the frequency of appendicitis in the rural districts and in the cities, showing that the frequency in the cities is more than a hundred times greater. Evidently appendicitis is a disease of higher civilization, where occupations are more sedentary. The five-fold increase in frequency with only a twofold increase, or less, in the death rate illustrates the more efficient surgical treatment and perhaps the tendency to greater morbidity in a country with state medicine.

We may also blame the physicians. Many of us are altogether too willing to please the patient and apply the icebag or heat and adopt a watchful waiting attitude. We know that many cases of appendicitis subside, but should another member of the family or the same patient have another attack, the same treatment will be applied and the result may be an appendicitis which proceeds to perforation.

There is no doubt that an increase has occurred in the number of appendicitis cases which go on to gangrene and perforation, due to delay in seeking competent medical and surgical advice. In the Pacific Northwest, the prevalence of cults and faith healers is to a great extent to blame. This has forcefully been brought to my attention lately, as illustrated by the following two cases.

CASE I. A girl, 20 years old, was seized with vomiting and abdominal pain. She went to a chiropractor who treated her with, "spinal adjustments," and massage over the abdomen for days. A surgeon was called and diagnosed the case as ruptured appendix with an abscess, and a secondary rupture of the abscess into the peritoneal cavity.

CASE II. A man 30 years of age developed abdominal pain, had a chiropractic treatment the following day, and took cathartics. On the seventh day the abdominal pain became so severe that he could no longer bear it and he then summoned me. I found a bulging over the right lower quadrant and rigid abdominal muscles.

He was brought to the hospital and operated on, the incision being made over the abscess which was found to have ruptured into the abdominal cavity. The intestines were bathed in thin, whey-like pus. On the second day gas bacillus infection in the abdominal wall became apparent. Death resulted from toxemia produced by the gas bacillus infection.

* Read before the Seattle Academy of Surgery, February 21, 1936.

In an editorial[1] in Surgery, Gynecology and Obstetrics, the statement is made that, "To operate in a case of spreading peritonitis invites catastrophe." The writer compares the condition with a skin or a subcutaneous progenic infection where the process is allowed to become localized and walled off before an incision is made for drainage. He states that the management of general peritonitis is identical.

It seems to me, however, that where we have a hollow viscus that becomes distended at the slightest provocation and especially when we have a peritonitis following a ruptured appendix, the thing to do is to relieve the distention and remove the cause if possible. It is important to reestablish the circulation as soon as possible, certainly before a paralytic ileus develops.

Gurd[2] states that, "the teaching, that the risk to the patient may be minimized by postponement of operation in the hope that a safe period may develop is to be condemned." My experience with a comparatively small series of cases leads me to believe that the postponement of the operation has very little in its favor. Draining an abscess and leaving the appendix in situ in selected cases is to be recommended. However, to do this as a routine will, I believe, cause an increase in the mortality rate and generally require reoperation. I have seen cases in which, years after drainage, appendiceal abscesses developed and caused death.

If nature has failed in its attempt to overcome the infection, if the appendix has ruptured, and abscess formation or spreading peritonitis or both have occurred, the best thing that can be done is for the surgeon to assist nature in its fight. From external examination it is almost impossible to tell the extent of the peritonitis. Everyone who has done any considerable abdominal surgery has made an incision in the upper abdomen or in the midline below the umbilicus, expecting to find the lesion there, only to find, to his surprise, an uninvolved peritoneal cavity in this location. Instead there will be a ruptured appendix in the right lower quadrant. Many such cases, treated medically as generalized peritonitis and reported as recovered, were in reality instances of circumscribed appendiceal abscesses, which may have ruptured into the cecum and drained themselves. There is only one way to treat appendicitis —early diagnosis and immediate operation.

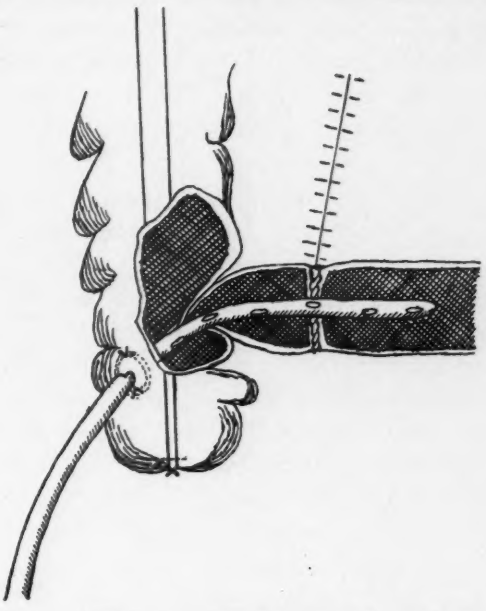

Fig. 1. Diagrammatic representation of the enterostomy tube in Case III. Where the tube is used for intestinal decompression in cases of gangrenous appendicitis with spreading peritonitis, the tube enters the cecum and ascending colon only.

In dealing with appendicitis which has developed into gangrene with peritonitis of varying extent, it is desirable to achieve a method of treatment which results in the smallest possible mortality and we feel that this is best done by aiding nature in its fight against the invading infection. In the abdominal cavity we find an easily distended viscus, whose distention cuts off the circulation to the intestinal wall by compression of its vessels. We can thus aid nature by deflating the viscus. The peritoneum has great power of withstanding and localizing any foreign invasion if there is no interference with circulation.

My method is to insert a No. 22 catheter through the appendix stump. If there is

much involvement at the base of the appendix, it is removed in the usual manner and another site on the cecum is used for the enterostomy. Where the appendix stump is being utilized, the catheter is fastened to it with a catgut suture. A purse-string suture is applied about the base of the appendix; it is invaginated around the catheter and the purse-string suture tied. A piece of omentum is placed about the catheter, and the latter is brought out through a stab wound lateral to the incision. The cecum may be anchored to the peritoneum. The enterostomy tube is fastened with silkworm gut to the skin. Adhesions which kink or bind down the bowel are released. Packs are used to protect the peritoneal cavity, if this can be done before the abscess is broken into. They are never put down through an infected area, since this merely helps to spread the infection. Abscesses are drained with gauze. Drains are never passed into an uninvolved portion of the peritoneal cavity, and they are never placed in the pelvis if pus is not found there at the time of the operation. Peritonitis travels by continuity.

The wound is closed in layers and the patient returned to the bed, where he is turned on his right side. The enterostomy tube is connected to a bottle, as in gall-bladder drainage.

I have always found this an effective means of keeping down the distention. The patient's postoperative course is much easier. There are no gas pains; the toxic intestinal contents are rapidly removed, and therefore there are fewer toxic manifestations. Since death in these cases is due to retroperitoneal infection and toxic absorption from the intestines, draining the intestines removes one factor. Administration of anaerobic antitoxin is also advisable.

The postoperative treatment of acute appendicitis with complications consists of constant attention to details. Daily rectal examination should be made. If abscesses develop, they should be drained through the rectum or, in women, through the posterior vaginal fornix. It is necessary to watch out for subhepatic or suphrenic abscesses. Nothing is to be given by mouth, but intravenous saline plus 5 per cent glucose should be administered as required, up to 3,000 c.c. a day. Subpectoral or hypodermoclysis may have to be used if the condition demands. No solution should be given per rectum and no enemas should be permitted. If there is gas in the distal portion of the colon, a rectal tube may be inserted. Constant heat to the abdomen, maintaining the patient in a semi-prone position to the right, and gastric lavage, if necessary, are valuable measures. Morphine may be given to avoid pain during the first few days. One must keep constant vigil to prevent complications from arising rather than to treat them after they have developed. The details of treatments should not be entrusted to nurses or interns if they have not been especially trained. The surgeon owes it to his patient to attend to the postoperative care himself.

CHART 1

Number of cases	75
Age range	4 to 65 years
Duration before operation	9 hours to 7 days
Incidence of gangrene, peritonitis and abscess	56
Gangrene and peritonitis with no localization	17 (1 death)
Gangrene and peritonitis with subphrenic abscess	2
Miscellaneous	
Five months' pregnancy	1 (Smooth convalescence. Delivered at term of healthy baby.)
Gas bacillus infection	1 (Died)
Postoperative complications	
Subphrenic abscess	2
Pulmonary abscess	1
Perinephritic abscess	3
Pelvic abscess	7
Morality	2.6 per cent

Chart 1 shows the findings in the series of cases here presented. The mortality rate is low; perhaps in a greater number of cases it would be increased several times.

There is no doubt that many surgeons object to the method of treatment advocated. Many men are deathly afraid of fecal fistula—but a fecal fistula which is open to the outside adds nothing to the risk, and is definitely beneficial. The

operative time is not much lengthened by the enterostomy procedure, while the easier postoperative course makes it certainly worthwhile. No greater tendency to postoperative hernia is exhibited than in any other treatment with drainage. The fistula heals by itself, as a rule. (This has been true in all my cases. In one, a boy 9 years old, the closure took place in two months after the patient was home and again in good health.)

The enterostomy method is not new, but I am convinced that lives have been saved by it.

In this small group of cases (seventy-five), all have been operated on immediately, or as soon as possible, after the diagnosis has been made. There has been no delay or attempt to establish a safe period by Ochsner's method or any other procedure. Where the appendix had not ruptured, or where abscesses or spreading peritonitis were not present, enterostomy was not done and the cases were excluded. There have been two deaths in the series.

The following case (not included in the series) illustrates the advantage of enterostomy and the ease with which it closes when properly performed. The acutely inflamed appendix in this case required no enterostomy, but there was obstruction with mesenteric thrombosis. The smooth and short convalescence in this serious case I attribute to the enterostomy.

Case III. A female, age 50, five years before had had what was supposed to have been an abscessed appendix which was drained. Her present illness began three days before admission with intermittent pain in the abdomen, which had gradually become worse. There had been no bowel movements for two days.

On examination, I found a moderately distended abdomen with visible peristalsis. There was a ventral hernia following the right rectus incision at the previous operation. The contents of the hernial sac could easily be reduced, but this did not affect the symptoms. The temperature was 100 and the pulse 90. My diagnosis was an obstructed bowel due to adhesions.

The patient was brought to the hospital and an incision was made just medial to the old scar. About 3 feet of the terminal ileum were found to be discolored, edematous and caught in a tight band. The mesenteric veins to the same portion were thrombotic. The last few inches of the ileum were not involved. The appendix was free, but acutely inflamed. There were no signs of any previous involvement about the appendix. We did a resection of the ileum together with the mesentery containing the thrombotic veins. An end-to-end anastomosis was made to the terminal portion of the ileum and the appendix was removed. A No. 32 catheter was inserted through an enterostomy in the cecum, through the ileocecal valve, and past the anastomosis. The hernia was repaired.

The patient made an uneventful recovery without distention or discomfort. The enterostomy tube was removed on the fifth day and the fistula was healed on the eighth. The patient left the hospital in two weeks and has remained well since.

SUMMARY

1. The frequency of appendicitis is increasing with advance in civilization.

2. Delay in seeking competent aid is the main factor in the mortality rate and medical treatment shares a portion of this responsibility.

3. The influence of cultism in the Northwest is also a factor.

4. Operative interference is recommended at time of diagnosis irrespective of the condition of the patient.

5. Removal of the appendix is necessary, with an enterostomy at the primary operation and drainage with gauze of the abscess cavities.

6. Antitoxin for anaerobic infection is administered in cases of ruptured appendix.

7. The right lateral position is best for drainage.

8. Careful postoperative management is advised, with the surgeon taking personal charge and making daily examinations.

REFERENCES

1. Editorial, *Surg., Gynec. & Obst.* May, 1932.
2. Gurd, F. B. *Am. J. Surg.*, 17: 52, 1932.
3. Mayo, Charles W. Appendicitis. In Collected Papers of the Mayo Clinic, 26: 154–162, 1934.

PRIMARY CARCINOMA OF THE LIVER*

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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PRIMARY carcinoma of the liver is comparatively rare, and a great deal that has been written on the subject is scattered among the pathologic and medical journals. However, the subject is by no means out of the realm of the surgeon. He encounters it during an exploratory laparotomy, only to find the peritoneal cavity full of blood from an eroded malignant nodule, or during an exploratory operation for an abdominal tumor of unknown origin. He is also confronted with it during an operation for "empyema of the gall-bladder," and sometimes a "gastric tumor" will turn out to be a primary tumor of the liver.

In order to study the prevalence of primary carcinoma of the liver, the autopsy records of thirty-one institutions of various countries were studied. The total number of autopsies collected was 159,762 (representing all deaths that came to autopsy). Of these, 808 were proved to be primary carcinoma of the liver, giving a percentage of 0.506. (Table I.) To the 808 cases are added 153 cases of primary carcinoma of the liver collected from the literature (Table II), where the ratio to the total number of autopsies was not given, and also 164 cases originally reported by Eggel in 1901, making a total of 1,125 cases of primary carcinoma of the liver reported in the literature up to August 1937. The ratio of primary carcinoma of the liver to all other malignancies is given as 8.4 per cent by Brines and 17 per cent by L. W. Smith (Philippine Islands), and 1.5 to 3 per cent by Jaffe. Of 3,300 malignant cases that came to necropsy at the Middlesex Hospital, as reported by Callwell, 41, or 1.2 per cent of all malignant diseases, were primary carcinoma of the liver. The proportion of primary to secondary carcinoma of the liver is given as 1 to 21 by Hale White, 1 to 64.5 by Orth, and 1 to 40 by Hansemann.

Primary carcinoma of the liver is more common in males than in females. In Eggel's series of 164 cases, 63.3 per cent occurred in males. The age incidence is the same as in any other malignancy. It is found at all ages. It may occur in infancy or childhood, but is most common after the age of forty. Muller reported a case of primary carcinoma of the liver in a man of 83. Griffith recorded fifty-seven cases under the age of 16. Dansie collected twenty-five cases under 2½. Although cancer in general is less common among colored races, primary carcinoma of the liver is more prevalent among them. Strong and Pitts reported twelve cases from the Vancouver General Hospital, ten of which occurred in Chinese. Tull reported 134 cases from the pathologic clinics of Singapore; 126 occurred in Chinese. Kika, in 1929, reported 110 cases of primary carcinoma of the liver from the Pathologic Institute of Tokio, and collected from the Japanese literature 223 cases since 1915. Von Hansemann examined 200,000 natives of the German colonies in Africa and found only twenty-one cases of all forms of cancer; four of these were primary carcinoma of the liver.

Pirie found ninety-six cases of all forms of cancer in South Africa, of which thirty-six were primary carcinoma of the liver. He attributed the disease to the prevalence of schistosomiasis among the natives. The parasite was found in 10 of the 36 cases. Pitts states that almost 100 per cent of the

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Table 1

RATIO OF PRIMARY CARCINOMA OF LIVER TO TOTAL NUMBER OF DEATHS THAT CAME TO AUTOPSY

Source	Number of Autopsies	Cases of Primary Carcinoma of Liver	Percentage
Barry and Russum. Creighton University School of Medicine	1,100	4	0.363
L. W. Smith. Philippines General Hospital	872	12	1.376
Berglund	1,312	16	1.219
Strong and Pitts. Vancouver General Hospital (1920–1931)	1,967	12	0.61
Goldzieher and Bokay. Path. Inst., Budapest	6,000	18	0.3
W. Hale White. Guys Hospital, London	18,500	24	0.129
Kika. Path. Inst. Tokio Univ., Japan	11,494	110	0.965
K. Smith. Cook County Hospital	4,044	25	0.618
Tull. Tan Tock Seng. Hospital, Singapore	17,664	134	0.758
Brines. Detroit Receiving Hospital (1929–1932)	1,087	8	0.736
Clawson and Cabot. Univ. Minnesota	5,100	1	0.019
Winternitz. Johns Hopkins Hospital	3,700	3	0.081
Wheeler. Guys Hospital, London	5,233	15	0.287
Von Glahn and Lamb. Presbyterian Hospital, New York	1,800	6	0.333
Rowen and Mollary. Boston City Hospital	6,506	9	0.138
Counseller and McIndoe. Mayo Clinic	5,976	5	0.083
Fried. Peter Bent Bingham Hospital	1,200	4	0.333
Fox and Bartels. State University of Iowa	1,500	2	0.133
Orth	258	4	1.55
Wilson. Roger Hospital, Charleston	818	2	0.244
Pirie. South African Inst. for Med. Research	91	36	39.56
Hansemann. Berlin Path. Inst. (1870–1889)	258	4	1.55
Chao-Jen Wu and Hsi-Jung Kang. Peiping Union Med. College	856	3	0.35
H. Collwell. Middlesex Hospital	12,500	41	0.328
H. Hill Univ. of Texas	150	3	2.0
Ciceri, Corso. Venice Hospital (1911–1931)	19,000	124	0.652
Cantele, P. G. City Hospital, Venice (1906–1929)	19,008	44	0.231
Yomone, M. Japan	2,503	57	2.277
Glynn, E. Liverpool Royal Infirmary (1922–1935)	2,050	16	0.78
Redaelli, P. Inst. Path. Anatomy, Univ. of Pavia	5,050	48	0.95
Hudimaki, Shigeo. Path. Inst., Niigata, Japan (1911–1935)	2,165	18	0.831
Grand totals	159,762	808	0.506

population in Kwantung (Southern China) are infected with intestinal parasites, the common fluke. Ascoli found that all his cases gave a history of syphilis, malaria or alcoholism.

Primary carcinoma of the liver occurs anatomically in three forms: the nodular, consisting of various circumscribed tumor nodules; the massive, composed of a large single tumor invading one of the lobes; and the diffuse, where the tumor process invades the whole liver substance. Histologically, they occur either as cholangiomas involving the intrahepatic bile ducts, or hepatomas arising from the parenchymatous liver cells. Hepatomas are most common and are most frequent in males. It is also known that cirrhosis of the liver is predominantly found in males. Cholangioma is most prevalent in females, perhaps due to the fact that bile duct infection is more common among females. Early vascular invasion of the intrahepatic blood vessels is a striking characteristic in hepatomas. Extrahepatic matastasis is most frequent in cholangiomas. Both may be associated with hypoglycemia or hemochromatosis. Jaffe reported a case of sarcoma and carcinoma of the liver in the same patient.

TABLE II
LIST OF CASES OF PRIMARY CARCINOMA OF THE LIVER REPORTED IN THE LITERATURE (NOT INCLUDED IN TABLE I

Author	No. of Cases	Author	No. of Cases
Boyce and McFetridge	28	Hicks	1
Glynn	16	Huguenin	1
Ulman and Loesch	10	Hustin	1
Karsner	9	Jackson	1
Hess	8	Jano and Matsuoka	1
Blumenau	7	Johnson and Hall	1
Ascoli	6	Karajanopoulos	1
Montanari	5	Koster and Kasman	1
Hill	4	LeGrand	1
Rugers	2	Liesch	1
Wilson	2	Margarot, Rimbaud and Guibert	1
Abel	1	Marono and Galand	1
Banet and Bolanas	1	Martinez	1
Barre and Paillas	1	Mast and Streamer	1
Beers and Morton	1	Moon	1
Benoit	1	Montpellier and Loubeyre	1
Blina	1	Müller	1
Bolker, Jacobi and Koven	1	Nadler and Waifer	1
Bosq and Pucher	1	Neuffer	1
Briggs	1	Orr	1
Brodin, Bolgert and Placa	1	Pallasse and Rougier	1
Cabot	1	Paviot, Martin, Gurchard and Girard	1
Calcagni	1	Peasley	1
Callerio	1	Plazy, Mondon and Berge	1
Catsaras	1	Prym	1
Crawford	1	Rosenthal	1
Ehrlich and Ansanelli	1	Schlomoritz and Glickman	1
Elliott	1	Schnabel	1
Finkelstein and Jacobi	1	Solowej	1
Finny and MacFarlane	1	Surbek and Vos	1
Gay	1	Thomson	1
Geschickter and Copeland	1	Trimarco and Behr	1
Goldberg and Wallerstein	1	Willis	1
Hedrick	1		
	120		34
Total	...		153

That cirrhosis of the liver plays an important part and is a predisposing factor in the formation of primary carcinoma of the liver is agreed by practically every writer on the subject. It is found in from 85 to 100 per cent of hepatomas and in 50 per cent of cholangiomas (Yamagiwa). Counseller and McIndoe questioned the diagnosis of primary carcinoma of the liver in the absence of definite cirrhosis. Blumenau made a study of 198 cases that died from cirrhosis. He found that 3.5 per cent of the series had primary carcinoma of the liver. Fried believes that cirrhosis is a reparative process in response to injury followed by hypertrophy and hyperplasia of liver cells, which gives rise to the formation of multiple adenomatous nodules which may eventually become malignant. Glynn describes a case where he found all three factors, hyperplasia, adenoma, and cancer in the same specimen. Muir states that the association of cirrhosis with cancer is much too frequent to be a mere coincidence. He agrees with Orth that the vicarious proliferative process for some unknown reason oversteps the normal and takes on the autonomous character of a new growth. That liver tissue has great powers of proliferation was proved experimentally by Podwyssowski and Mann. The latter removed 70 per cent of the liver in animals, and this was followed by practically complete regeneration in the course of a few months.

Cirrhosis in itself may be secondary to syphilis, alcoholism, malaria, parasitic and infectious diseases. Of the sixteen cases reported by Glynn, five had biliary calculi. Cases have been reported by Hicks, Crawford and Calcagni that gave a history of direct trauma before the appearance of the symptoms.

Intrahepatic metastasis is quite frequent. The intrahepatic veins are almost always involved, forming small thrombi which may extend to the larger veins and inferior vena cava and right auricle, as shown in the cases of Winternitz, Counsellor and McIndoe, and Barry and Russum.

In spite of early vascular involvement, extrahepatic metastasis is not frequent. When it does occur, it is most common in the lungs, mediastinum and upper abdominal lymph glands. Twenty per cent of all primary carcinomata of the liver metastasize to the lungs. Metastasis into the sac of an inguinal hernia was reported by R. A. Willis. Jano and Matsuoka reported a patient who died from cardiac failure caused by hydropericardium and ascites. Autopsy revealed a primary bile duct carcinoma of the liver, with massive pericardial effusion from multiple cardiac metastases. Peasley reported a case of primary carcinoma of the liver with invasion of the portal and hepatic veins and

gangrene of the small intestine. Bolker, Jacobi and Koven in 1937 collected from the literature nine cases of primary carcinoma of the liver with skeletal metastis and reported one of their own. To these are added the three cases of K. J. Smith, one of Counsellor and McIndoe, two of Surbek and Vos, one of Thomson, and one of Hedrick, making a total of eighteen cases of primary carcinoma of the liver with skeletal metastasis, or 1.6 per cent of the total number of cases of primary carcinoma of the liver reported in the literature up to the present writing. The comparative freedom from metastasis in spite of early thrombosis may be due to the short duration of the disease. The patient is dead before distant metastasis takes place.

Fig. 1. Low power magnification of a representative section of liver. A, persisting cords of normal liver cells spread apart by edema. B, a nest of regenerating liver cells surrounded by scar. C, regenerating liver cells merging indefinitely with neoplastic masses. D, a mass of malignant liver cells occupying the lumen of a periportal blood vessel.

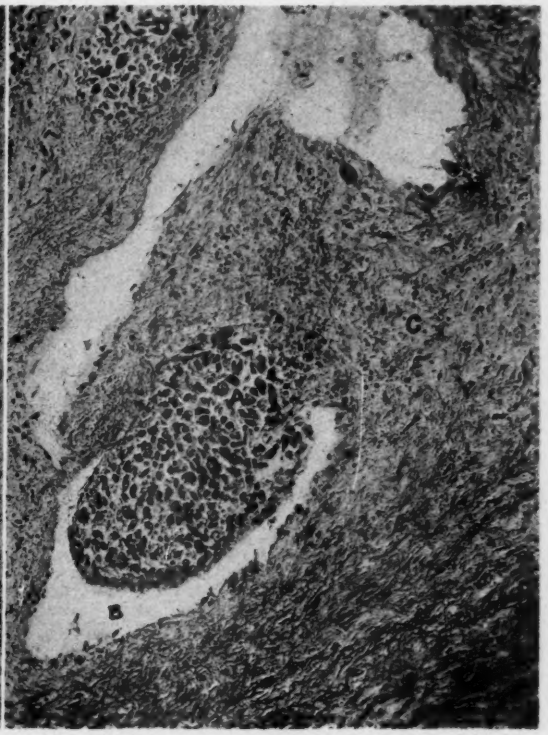

Fig. 2. High power magnification through a characteristic area of the hepatoma. A, the mass of malignant liver cells, including giant cells growing into B, the lumen of a blood vessel. C, the dense scarring of periportal areas accompanied by round cell infiltration. D, a nest of malignant cells adjacent to and occupying portion of the vessel wall.

There are no pathognomonic symptoms or signs in primary carcinoma of the liver to enable one to make a positive diagnosis. In the early stage, the patient will complain of vague gastrointestinal disturbance, nausea, sometimes diarrhea, anorexia and weakness, and later progressive loss of weight. He then develops signs and symptoms of atrophic cirrhosis. The abdomen becomes distended, the superficial abdominal veins are engorged. Ascites develops in about 58 per cent of cases, jaundice in 61 per cent, with edema, especially of lower extremities in 41 per cent (Eggel's statistics). When an abdominal paracentesis is done, the liver is seen and felt below the costal margin, sometimes as low as the umbilicus. The characteristic of liver enlargement, however, is upward into the thorax, as seen by roentgenogram examination of the chest and on percussion. Mallory's patient (#22051) had an explora-

tory operation of the right chest for a mediastinal tumor and it was discovered that the tumor was a primary hepatoma pushing the diaphragm high into the chest cavity. Of 134 cases reported by Tull, in fifty-two the dome of the liver was pushed up into the thorax, sometimes as high as the third rib. Pain and dyspnea depend on the pressure of the tumor mass upon the adjacent structures.

Diagnosis is often missed even after exploratory operation and the taking of a biopsy. The biopsy will be reported as cirrhosis, and so it is, but the patient has associated with the cirrhosis primary carcinoma of the liver. Various liver function tests are of no avail in carcinoma, for many other liver diseases will give the same results. Few of the cases reported have been diagnosed clinically. The records of the past have been based on necropsy findings and on operative removal of a malignant tumor after surgical exploration.

The treatment of primary carcinoma of the liver is exclusively surgical. There is no other choice of treatment. This is one type of malignancy which is out of the realm of radiology. When one takes into consideration that the duration of life after the appearance of the tumor is about three months, the mortality following operation, even when very high, is not of such great consequence as in other types of less fatal malignant disease. It is generally agreed that every case of primary carcinoma of the liver should be explored, but this should be done not only for diagnostic purposes and the taking of a biopsy, but also with the idea of a possible excision of a solitary malignant tumor or even a lobectomy. The fact that the blood supply of each lobe is practically distinct and the amount of connective tissue very abundant, bespeaks its safety. Wright states, "I think that the simple method of cutting boldly through the liver tissue is quite safe."

In reporting a case of resection of the left lobe of the liver for primary carcinoma, Keen in 1899 collected from the literature seventy-six cases of resection of the liver for hepatic tumors. Sixty-three recovered, eleven died, and the termination of two was uncertain, giving a mortality of 14.9 per cent. Keen asked, "If we cure 50 per cent of cases of cancer of the breast and over 50 per cent of cases of cancer of the rectum and uterus, why should we not get equally good results at least in these cases of cancer of the liver which are well limited and with little or no lymphatic involvement?" He concluded that every case, saving those manifestly beyond relief, should therefore be explored and the later steps be determined by what is found. Thomson notes with surprise that in his collection of forty-seven cases from the literature of neoplasms of the liver that have been operated on, only two died from hemorrhage, and in the forty-seven cases there were only six deaths.

Yeoman in 1915 reported a case of primary carcinoma of the liver in which he operated for recurrence over seven years after the primary operation. He collected from the literature fifteen other cases of primary carcinoma of the liver in which there had been operations. Of these, four died from various causes within sixteen days after operation, six had a recurrence in from two months to eight years after operation, and six were alive and well from three to seven years after operation. He concludes that the only hope for improvement in results lies in the direction of earlier operative exploration in patients with tumors in the right upper quadrant in whom no primary growth can be found.

Table III shows fourteen additional cases of malignant tumor of the liver operated on since the reports of Keen, Thomson and Yeoman. (Hemangiomas, gumma and cystic tumors of the liver are omitted.)

REPORT OF CASE

A 30 year old Philippine male was admitted to Cumberland Hospital on March 31, 1935 complaining of intermittent sharp, shooting pain in the right upper quadrant, right chest, shoulder and axilla, and soreness in the epigastric region of four weeks' duration. The pain was relieved on deep respiration.

TABLE III

SUMMARY OF FOURTEEN CASES OF CARCINOMA OF THE LIVER WHERE OPERATION ON THE LIVER WAS PERFORMED

Sex and Age	Pathology	Operative Findings	Method of Removal	Results	Author
Male 13	Tumor weight 2 lbs. 3 oz. Hepatic adenoma.	Lobulated tumor occupying almost one half of right lobe of liver. No other organs involved.	V-shaped incision, apex at cystic duct. Gall-bladder removed with tumor after ligating cystic duct and vessels. Stomach clamp, knife and scissors, long intestinal needle and chromic No. 3 used. Edges approximated.	Excellent health one year and ten months after operation. Working.	Turner, Grey
Male 60	Tumor partially encapsulated. Liver cell carcinoma.	Tumor size of orange in right lobe of liver. Thought to be primary carcinoma.	Tumor shelled out after removing gall-bladder. Bleeding controlled by pressure and swab. Vessels clamped and ligated. Wound packed with gauze.	Well three years after operation.	Wright, G.
Female 40	Carcinoma.	Carcinoma of gall bladder, stones, malignant module of liver.	Excision by scalpel of wedge of liver with gall-bladder, measuring 3 × 3½ × 2 inches. Bleeding controlled by digital pressure and gauze. Gap filled with omentum. Sutures passed through omentum and liver. Omentum later detached from main omental sheath.	Well after fifteen months. Could not be traced later.	Frankau, C.
Female 29	Adenoma of the liver.	Peritoneal cavity full of blood. Pelvic organs normal. Large cone-shaped tumor at inferior surface of right lobe of liver. Rent 3 inches in tumor from which blood was escaping. First thought to be ectopic pregnancy.	Tumor removed by cautery.	Died one hour after operation.	Turner, P.
Female 57	Adenoma of the liver.	Preoperative diagnosis subacute appendicitis. Tumor size of cricket ball in right lobe of liver.	Splinting sutures. Wedge-shaped area removed with tumor.	Patient did well but died from "heat stroke."	Kidd, F.
Female 54	Carcinoma of adrenal rest.	Yellowish tumor of lingual lobe of liver.	Clamped, resected, mattress sutures applied.	Lived two years after operation.	Nitch, C. A. R.
Female 80	.....	Tumor occupying almost the entire left lobe of liver, measuring 16 × 12 × 12 cm.	Tumor resected after left hepatic artery and vein ligated.	Patient in good health seventeen months later.	Jackson, R. H.

TABLE III (*Continued*)

Sex and Age	Pathology	Operative Findings	Method of Removal	Results	Author
Male 35	Primary carcinoma of liver.	Two tumors size of grapefruit at under surface of left lobe by pedicle. No other involvement.	Clamped, cut, sutured.	Well eleven months later. Gained 22 lbs.	Goldberg, Wallerstein.
Male 51	Cholangioma. Tumor 8½ × 6½ × 4 in. 3 lbs. 11 oz.	Large tumor at left lobe of liver.	Practically the whole lobe was removed. Series chromic No. 2 sutures passed through whole substance of liver and tied. Tumor with 1 inch of normal tissue removed. Practically the whole left lobe of liver removed.	In good health seven months after operation.	Abel, A. L.
Male 43	Encapsulated tumor with central degeneration. 9 × 8 × 7 cm. Primary carcinoma.	Encapsulated tumor left lobe of liver, size of orange. Embedded in a "band of cirrhosis" 2 inches wide.	Excised by sharp dissection. Cut surface sewn as cut with interlocking double catgut.	Died six months after operation.	Hicks, E. S.
Male 59	Hepatoma. Autopsy findings metastasis to right lobe, peritoneum, heart.	Large tumor involving the left lobe. No other foci.	Partial resection of left lobe, portal vein and hepatic artery clamped and tied. Remainder of left lobe removed by electric cautery.	Died six weeks after operation.	Love
Male 51	Adenocarcinoma of the liver.	Large cystic tumor involving left lobe of liver, filled with blood clots and macerated liver tissue.	Tumor resected, blood vessels clamped and tied. Cut surface of liver approximated with catgut.	Patient in good health nine months after operation.	Hustin, A.
Male 43	Primary carcinoma of the liver.	Malignant nodule at free border of liver. All other organs normal.	Malignant nodule, gallbladder with wide margin of normal tissue excised.	.....	Le Grand
Female 44	Tumor weight 940 Gm. Adenocarcinoma.	Large tumor involving most of right lobe of liver.	Excision.	Alive nine years after operation.	Wendel, W.

Two years previous he was admitted to a hospital for "stomach trouble" and had a gastrointestinal series done. As the series was negative, he was discharged. Ever since, fried foods, meats and fats gave him a great deal of flatulence, nausea, and pain in the epigastric region. He had gonorrhea in 1925, but otherwise he had never been sick. He had an occasional cough with no expectoration and no hemoptysis, and also a slight orthopnea. He used to drink a large quantity of alcoholic beverages until two years previous, when he had developed "stomach trouble." His family history was essentially negative.

Examination revealed a 30 year old Philippine male, moderately nourished, not acutely ill, comfortable. His temperature was 101°F., pulse 80, respiration 24, blood pressure 124/72. The head and neck did not reveal any abnormality. The chest showed signs of dul-

ness and flatness over the right base with suppressed breath sounds and occasional râles. There was no evidence of any abnormality of the heart.

The abdomen was asymmetrical and slightly distended, with a moderate amount of edema of the skin. The superficial abdominal veins were engorged. The right upper quadrant was very prominent. The upper border of liver dulness extended to the fourth interspace. The liver edge was palpated three fingers below the costal margin (very tender), while the left lobe extended to the left costal margin. The spleen was not palpable nor were any other masses palpable. There was a 2 plus edema of both ankles and the lower third of the legs.

The urine showed a slight trace of albumin with no bile present. The blood Wassermann was negative. A blood chemistry indicated 15 mg. urea nitrogen, 1.7 mg. creatinine, 3 mg. of uric acid, and 80 mg. of sugar. There were 8,750 white cells with 77 per cent polymorphonuclear leucocytes and 28 per cent lymphocytes; the hemoglobin was 60 per cent. The icteric index was 6.1; the Van den Bergh test was negative. The stool examination was positive only for blood, and contained only Bacillus coli. The Takata-Ora test was positive. The gastric analysis was normal. A flat plate of the abdomen showed the lower border of the liver about 6 cm. above the intercostal line. Roentgenogram of the lungs showed no infiltration or consolidation. Sedimentation time was 35 minutes.

On April 22 the abdomen became more distended and slightly rigid, while a cystic mass was felt over the right lobe of the liver. The patient did not do so well. On April 24 an exploratory laparotomy was performed by Dr. Merrill N. Foote. Upon the opening of the peritoneum, the abdomen was found filled with blood, blood clots, and hemorrhagic ascitic fluid. The superior and inferior surfaces of the liver were covered with circumscribed bluish areas simulating localized hemangiomas. The bleeding came apparently from the superior surface of the liver and could not be exposed. The liver surface was packed with iodoform gauze after removal of the clots and removal of the fluid by suction. A biopsy was taken from the anterior border of the liver and the edges were approximated with chromic No. 2. The abdomen was then closed in the usual manner. The patient did not do so well after the operation, but improved after stimulants and a transfusion of 500 c.c. of blood. However, two days later, on April 26, he died. As the biopsy from the liver was reported as cirrhosis, he was signed out with that diagnosis.

Autopsy performed by Dr. S. H. Polayes disclosed that the peritoneal cavity contained about 2,000 c.c. of blood and several large clots in the right gutter. The omentum was adherent to the superior surface of the right lobe of the liver. On removing the omentum from that area, a degenerated, necrotic, "abscess-like" cavity was disclosed, measuring about 5 cm. in diameter, containing necrotic slough. The omentum partially sealed this cavity. The liver was tremendously enlarged, weighing more than 3,200 Gm. The entire right lobe appeared necrotic and hemorrhagic. On section through the abscess-like area, the tissue appeared cystic, containing dark, chocolate, reddish colored fluid of purulent consistency. The area immediately surrounding the mass was red, soft, and necrotic, involving a large part of the right lobe. The left lobe contained fairly normal liver structure with areas of fat replacement.

On microscopic examination, the more normal portion of the liver showed evidence of destruction of the hepatic lobules, increase in the number of bile capillaries, replacement of liver cells by connective tissue and evidence of regeneration of liver cells. The section of the right lobe of the liver which was the seat of the neoplastic involvement showed large areas of necrosis, cystic degeneration, and hemorrhage. There were large numbers of nests of neoplastic liver cells among which were numerous giant cells with nuclei undergoing mitosis. There was complete absence of normal liver tissue.

Glisson's capsule was the seat of an inflammatory process with round cell infiltration. The rest of the abdominal viscera showed no evidence of pathology.

The visceral and parietal pleura were densely adherent to each other and the adhesions were separated with difficulty. On section the right lung showed lobular patches and pneumatic consolidation. Histologic examination revealed the presence of miliary tubercles and areas of lobular pneumonia.

The final diagnosis was hepatoma, miliary tuberculosis of the lungs, lobular pneumonia, pleural fibrosis, peritoneal hemorrhage, aortic atherosclerosis.

SUMMARY

1. Primary carcinoma of the liver is comparatively rare.

2. There is very little written on this subject in the surgical literature.

3. An exhaustive review of the literature on the subject was made, and 1,125 cases were found to have been reported.

4. The pathology and the clinical course of the disease are discussed.

5. A plea for more surgical interference in primary carcinoma of the liver is made, through the medium of men in the past who are more qualified to speak on the subject.

6. A table is included containing a summary of fourteen cases that have been operated on for primary carcinoma of the liver.

7. An additional case of primary carcinoma of the liver complicated by miliary tuberculosis is reported.

8. References are included, comprising practically everything that has been written on the subject.

REFERENCES

1. Abel, A. L. *Brit. J. Surg.*, 21: 684, 1934.
2. Ascoli, D. M. *Policlinico*, 37: 309, 1930.
3. Banet, V., and Bolanas, J. M. *Bol. liga. contra. el cancer*, 8: 7, 1933.
4. Barre, J. A., and Paillas, J., *Marseille méd.*, 1: 159, 1934.
5. Barry, M. W., and Russum, B. C. *Nebraska M. J.*, 16: 312, 1931.
6. Beers, D. N., and Morton, J. J., *Am. J. Cancer*, 24: 51, 1935.
7. Benoit, E. P. *Union méd. du Canada*, 60: 85, 1931.
8. Berglund. Quoted by Strong and Pitts. *Arch. Int. Med.*, 46: 105, 1930.
9. Blina, Luciano. *Clin. med. ital.*, 62: 99, 1931.
10. Blumenau, E. *Arch. f. Verdauungskrank.*, 27: 1, 1920.
11. Bolker, J., Jacobi, M., and Koven, M. T. *Ann. Int. Med.*, 10: 1213, 1937.
12. Bosq, P., and Pucher, E. *Semana med.*, 2: 132, 1935.
13. Boyce, F. F., and McFetridge, E. M. *Internat. Surg. Digest*, Critic Section, Dean Lewis Practice of Surgery, 18: 67, 1934.
14. Briggs, J. F. *Minnesota Med.*, 16: 230, 1933.
15. Brines, O. A. *Am. J. Clin. Path.*, 3: 221, 1933.
16. Brodin, P., Bolgert, M., and Placa, A. *Ann. d'anat. path.*, 12: 355, 1935.
17. Cabot. *New England J. Med.*, 203: 80, 1930.
18. Calcagni, A. C. *Clin. Chir.*, 36: 311, 1933.
19. Callerio, G. *Riv. di clin. med.*, 32: 45, 1931.
20. Callwell, H. *Arch. Middlesex Hosp.*, 5: 122, 1905.
21. Cantele, P. G. *Tumori*, 5: 233, 1931.
22. Catsaras, M. J. *Ann. de méd.*, 10: 295, 1921.
23. Chao-Jen Wu, and Hsi-Jung Kang. *Nat. M. J. China*, 16: 234, 1930.
24. Ciceri, C. *Gass. Interaz. Med.-Chir.*, 39: 72, 1931.
25. Clawson, and Cabot. *J. A. M. A.*, 80: 909, 1923.
26. Counseller, V. A., and McIndoe, A. H. *Arch. Int. Med.*, 37: 363, 1926.
27. Crawford, W. H. *Am. J. M. Sc.*, 181: 496, 1931.
28. Dansie, C. B. *Lancet*, 2: 228, 1929.
29. Eggel, H. *Beitr. z. path. Anat.*, 30: 506, 1901.
30. Ehrlich, D. E., and Ansanelli, F. C. *J. A. M. A.*, 105: 355, 1935.
31. Elliott, C. A. *Tr. A. A. Physicians*, 44: 121, 1929.
32. Finkelstein, R., and Jacobi, M. *Ann. Int. Med.*, 7: 1919, 1934.
33. Finny, C. M., and MacFarlane, L. R. S. *J. Roy. Army Med. Corps*, 68: 117, 1937.
34. Fox, R. A., and Bartels, G. W. *Arch. Path.*, 6: 228, 1928.
35. Frankau, C. *Proc. Royal Soc. Med.*, 16: 59, 1923.
36. Fried, B. M. *Am. J. M. Sc.*, 168: 242, 1924.
37. Gay, G. *J. Missouri M. A.*, 28: 157, 1931.
38. Geschickter, C., and Copeland, M. Tumors of bone. *Am. J. Cancer*, p. 545, 1936.
39. Glynn, E. *Brit. M. J.*, 11: 1192, 1911.
40. Goldberg, S. J., and Wallerstein, H. *Rev. Gastroent.*, 1: 305, 1934.
41. Goldzieher, M., and Bokay, Z. *Virchows Arch. f. path. Anat.*, 203: 75, 1911.
42. Griffith, J. F. C. *Am. J. M. Sc.*, 160: 79, 1918.
43. Hale and White. Allbutts System of Medicine. 4: 215, 1910. New York, 2nd ed. MacMillan.
44. Hansemann. *Berlin klin. Wchnschr.*, 27: 353, 1890.
45. Hedrick, D. W. *J. Bone & Joint Surg.*, 19: 817, 1937.
46. Hess, L. *Wien. klin. Wchnschr.*, 47: 1129, 1934.
47. Hicks, E. S. *Canad. M. J.*, 20: 169, 1929.
48. Hill, H. *Texas State J. Med.*, 25: 14, 1929.
49. Hudimaki, Shigeo. *Gann*, 30: 685, 1936.
50. Huguenin, B. *Zentralbl. f. allg. Path. u. path. Anat.*, 22: 241, 1911.
51. Hustin, A. *Bull. et. mém. Soc. nat. de chir.*, 56: 940, 1930.
52. Jackson, R. H. *Tr. South. Surg. A.*, 44: 299, 1931.
53. Jaffe, R. H. *Arch. Int. Med.*, 33: 330, 1924.
54. Jano, Y., and Matsuoka, K. *J. Oriental Med.*, 19: 115, 1933.
55. Johnson, L. W., and Hall, W. W. *U. S. Naval Med. Bull.*, 31: 31, 1933.
56. Karajanopoulos, G. *Bull. Assoc. franç. pour l'étude de cancer*, p. 90, 1912.
57. Karsner, H. T. *Arch. Int. Med.*, 8: 238, 1931.
58. Keen, W. W. *Ann. Surg.*, 30: 267, 1899.
59. Kidd, F. *Proc. Roy. Soc. Med.*, 16: 61, 1923.
60. Kika, G. *Gann*, 23: 107, 1929.
61. Koster, H., and Kasman, L. P. *Am. J. Surg.*, 17: 237, 1932.
62. LeGrand. *Normandie méd.*, 43: 58, 1932.
63. Liesch, E. *Riv. de clin. med.*, 32: 218, 1931.
64. Love, R. J. *Brit. J. Surg.*, 22: 387, 1934.
65. Mallory, Tracy B. *New England J. Med.*, 214: 209, 1936.

66. Mann, F. C. *Am. J. M. Sc.*, 37: 101, 1921.
67. Margarot, J., Rimbaud, P., and Guibert. *Bull. Soc. franç. de dermat. et syphilog.*, 42: 1486, 1935.
68. Marono, A., and Galand, J. B. *Semana med.*, 1: 1805, 1932.
69. Martinez, J. A. *Lancet*, 2: 1293, 1935.
70. Mast, W. H., and Streamer, C. W. *J. A. M. A.*, 100: 1684, 1933.
71. Montanari, A. *Riv. di clin. med.*, 33: 283–299, 345–369, 398–418, 1932.
72. Montpellier, J., and Loubeyre, J. *Bull. Soc. franç. de dermat. et syphilog.*, 40: 304, 1933.
73. Moon, V. H. *Arch. Path.*, 8: 938, 1929.
74. Muir, R. *J. Path. & Bact.*, 12: 287, 1908.
75. Muller, W. *Zentralbl. f. allg. u. path. Anat.*, 61: 161, 1932.
76. Nadler, W. H., and Waifer, J. A. *Arch. Int. Med.*, 44: 700, 1929.
77. Neuffer, H. *Zentralbl. f. Chir.*, 58: 719, 1931.
78. Nitch, C. A. R. *Lancet*, 1: 334, 1923.
79. Orr, J. W. *Lancet*, 1: 1400, 1930.
80. Orth, M. Ueber Leberkarzinome. Strassburg, 1885.
81. Pallasse, and Rougier. *Lyon méd.*, 148: 548, 1931.
82. Paviot, J., Martin, J. E., Gurchard, A., and Girard. *Lyon méd.*, 154: 508, 1934.
83. Peasley, E. D. *Bull. Truesdale Hosp.*, 5: 25, 1931.
84. Pirie, J. H. *M. J. South Africa*, 17: 87, 1921.
85. Plazy, L., Mondon, H., and Berge, C. *Bull. Assoc. franç. pour l'étude du cancer*, 24: 471, 1935.
86. Podwyssowski. *Beitr. z. path. Anat. u. z. allg. Path.*, 1: 259, 1886.
87. Prym, P. *Frankfurt. Ztschr. f. Path.*, 10: 170, 1912.
88. Redaelli, P. Epatiti parenchimatose, epatiti interstiziali chroniche e tum. epith. del feg., tip. coop. Pavia, 1926.
89. Rosenthal, S. R. *Arch. Path.*, 13: 88, 1932.
90. Rowen, and Mollary. *Am. J. Path.*, 1: 677, 1925.
91. Rugers, H. *Am. J. Cancer*, 15: 2386, 1931.
92. Schlomoritz, B. H., and Glickman, L. G. *Wisconsin M. J.*, 33: 841, 1934.
93. Schnabel, T. G. *Ann. Surg.*, 101: 613, 1931.
94. Smith, K. *J. Lab. & Clin. Med.*, 18: 915, 1932.
95. Smith, L. W. *Arch. Path.*, 1: 365, 1926.
96. Solowej, M. *Ztschr. f. Krebsforsch.*, 33: 442, 1931.
97. Strong, G. F., and Pitts, H. H. *Ann. Int. Med.*, 6: 485, 1932.
98. Surbek, K. E., and Vos, J. J. Th. *Geneesktijdschr. v. Nederl.-Indie*, 75: 239, 1935.
99. Thomson, J. E. *Ann. Surg.*, 30: 284, 1899.
100. Thomson, S. A. *Canad. M. A. J.*, 32: 675, 1935.
101. Trimarco, J. R., and Behr, O. J. *Prensa med. argent.*, 21: 1818, 1934.
102. Tull, C. J. *J. Path. & Bact.*, 35: 557, 1932.
103. Turner, Grey. *Proc. Roy. Soc. Med.*, 16: 43, 1923.
104. Turner, Ph. *Proc. Roy. Soc. Med.*, 16: 60, 1923.
105. Ulman, J., and Loesch, J. *Bull. Med. Soc. County of Erie and Buffalo Acad. Med.*, 9: 20, 1932.
106. Von Glahn, W. C., and Lamb, A. R. *M. Clin. North America*, 8: 29, 1924.
107. Wendel, W. *Arch. f. klin. Chir.*, 114: 982, 1920.
108. Wheeler, F. J. *Guys Hosp. Rep.*, 48: 225, 1909.
109. Willis, R. A. *M. J. Australia*, 17: 606, 1930.
110. Wilson, R. *Internat. Clin.*, 3: 157, 1931.
111. Winternitz, M. C. *Johns Hopkins Hosp. Rep.*, 17: 143, 1916.
112. Wright, Garnett. *Proc. Roy. Soc. Med.*, 16: 56, 1923.
113. Yamagiwa, K. *Virchows Arch. f. path. Anat.*, 206: 437, 1911.
114. Yeomans, F. J. *J. A. M. A.*, 64: 1301, 1915.
115. Yomone, M. *Verhandl. d. Jap. Path. Gesellsch.*, 8: 259, 1918.

THE MANAGEMENT OF CHRONIC OCCLUSIVE PERIPHERAL ARTERIAL DISEASE

IMPRESSIONS GAINED FROM SIX YEARS OF CLINICAL STUDY

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CHRONIC occlusive arterial disease unfortunately is widespread among the adult populace. Its progression is attended with dire results; its complications are often serious, not infrequently fatal. Too often the practitioner is unmindful of the seriousness of the affection, and at times even of its nature.

Every patient with complaints referable to the peripheral arteries should have a thorough physical examination. The presence or absence of diabetes must be definitely established. The peripheral circulation should then be carefully studied by one fully versed in the anatomy and physiology of the peripheral vessels. The part played by the autonomic nervous system should be determined by a quantitative measurement of the degree of vasoconstriction, using an accepted method of vasomotor study. The writer prefers peripheral nerve conduction block as the most reliable method of inducing vasoconstrictor paralysis. His experiences with this method will be reported in an article to follow. One cannot expect the general practitioner to be versed in the details of a thorough vascular study; but his lack of training in this respect is no excuse for denying this to the patient when a vascular surgeon is within reach.

The chronic arterial occlusion may be due to arteriosclerosis, thrombo-angiitis obliterans, endarteritis obliterans, or other more rare affections. Irrespective of etiology, the important manifestations are the result of diminished blood flow. In each group, the goal in treatment is to increase the available circulation to the affected limb. There are at present no well recognized specific means of treatment of the various types of occlusive arterial disease. To a great extent, rational treatment depends on the results of the vasomotor study.

If there is little or no vasoconstrictor element, the use of drugs or other means directed towards the decrease of sympathetic influence is not indicated. Suction pressure therapy has been strongly advised by others for this group. The writer has had experience with approximately 5,000 hours of suction pressure treatment. Most of the cases were proved by vasomotor studies to have little or no element of vasoconstriction. A few patients have reported worthwhile results, some only temporary; in the majority, however, the results have been most disappointing. The use of intravenous hypertonic salt solution, adrenalin-free pancreatic extract, padutin, and other drugs, has met with little success in the author's hands in relieving symptoms or altering the course of the disease.

Gratifying results have been obtained in a small series of patients treated by ligation of the main vein to the extremity. Patients for vein ligation must be carefully selected; they should have little or no element of vasoconstriction and should show only mild evidence of circulatory incompetency. Following vein ligation the surface temperature of the extremity has shown a persistent increase, and both symptoms and objective findings have shown improvement. However, it is useless to attempt this procedure in advanced cases of arterial disease.

Circulatory postural exercises as advised by Buerger and carried out systematically

for three hours daily are of distinct benefit. The writer has had no experience with intermittent venous compression as recently advised by Collens and Wilensky. Strict daily hygiene of the feet must be a part of the management of every case. The skin must be kept soft, clean, and free of trauma. If the skin is broken, care must be exercised to keep the lesions aseptic, with the scrupulous avoidance of strong antiseptics such as tincture of iodine.

Most cases of ulceration or gangrene due to arterial disease show little or no vasoconstriction. Certain points in the treatment of these cases are worthy of mention. The involved extremity should not be elevated as a routine—I have no doubt that many extremities are sacrificed because this antiquated outworn dictum is rigidly followed. The extremity should be kept at its optimum level, obtained by elevating the extremity for a few minutes until it blanches and then slowly lowering it until the normal pink color is present. The patient usually feels more comfortable at this point. In most cases the optimum level is slightly lower than the horizontal. If there is a suppurative lesion, its site should hang dependent to promote drainage, even if this requires placing the patient in the supine position.

The extremity should be kept warm, but great care must be exercised in the use of electric lights or appliances. I have seen extremities sacrificed and even death result from burns produced by electric heating devices, so that I no longer countenance the use of electricity for this purpose. The methods of heating must be absolutely fool-proof. The degree of heat must not be gauged by the sensations of the patients, for his extremity may be anesthetic or hypesthetic. No form of heat should be applied unless a sensory examination has been previously made.

The extremities must be so placed that there are no areas of pressure; the heels must be kept scrupulously away from the mattress, and the patient's bed should be fitted with a Balkan frame with a hand trapeze, so that he can move himself without using his heels. The cradle which covers the extremities should be thoroughly padded to prevent mechanical injury. Constant vigilance by the physician himself is necessary to prevent calamities occuring during the course of treatment. To be suddenly aware that due to pressure a gangrenous spot has appeared on the heel of the less involved extremity is often evidence of neglect, and most embarrassing. One must not be so eager to treat the obvious lesion that his attention is withheld from the danger of such complications in the "good" but often poorly nourished fellow opposite.

In those cases where the occlusive disease is accompanied by a marked or considerable element of vasoconstriction, best results are obtained by releasing this factor. In the author's experience, the use of vasodilatory drugs, by mouth, injection, or iontophoresis; contrast or cold baths, diathermy to the sympathetic chains or the affected extremities, or vaccine fever have not been promising.

Sympathetic ganglionectomy will produce an increased circulation to the affected extremities, at least to the extent indicated by the vasomotor studies; and this increase will persist at the maximum test level or slightly below it for an extended period. The increased blood flow is present continuously, day and night, and is more marked and more persistent than that obtained by any other means known to the writer. The vasodilatation acts to prevent or lessen the incidence of thrombosis and occlusion in vessels not already totally occluded, striking a well directed blow at the site of the disease. It forms the most efficient basis for the encouragement of collateral circulation.

Some claim that this effect is not permanent. Four years ago, however, the author first performed lumbar ganglionectomy for chronic occlusive arterial disease of the lower extremities with a large element of vasoconstriction in a patient age 47, with a pregangrenous toe.

The resultant vasodilatation has persisted at almost the normal level to the present time, and is attended with remarkably satisfactory results.

In the upper extremities the results are sometimes not quite so good as in the lower extremities, but the persistence of vasodilatation for an extended period is of great benefit and not obtainable otherwise. There are those who look with disfavor on ganglionectomy for these conditions, and it is true that the claudication is in many cases not thus relieved. However, those who have seen the disappointing results of other methods of treatment over a period of years, cannot deny that no procedure offers the degree of increased circulation obtainable by ganglionectomy in the properly selected case. No procedure offers greater insurance against the serious complications of progressive arterial disease. If ganglionectomy is to be done, it should be done early, because as the disease progresses the vasoconstrictor element gradually recedes. In thrombo-angiitis obliterans ganglionectomy should be promptly done on the less involved extremity as a prophylactic measure since the disease becomes bilateral in about 95 per cent of cases.

The operation of lumbar ganglionectomy as developed by the author[1] through a completely muscle-splitting extraperitoneal approach is easily and quickly performed by trained hands with very little danger to the patient. The period of hospitalization is shortened by this approach to five or six days. For the upper extremities the "preganglionic operations" are now in favor and the results are very promising.

[1] Pearl, Felix L. Muscle-splitting extraperitoneal lumbar ganglionectomy. *Surg., Gynec. & Obst.*, 65: 107, 1937.

SUMMARY

1. There are no effective well-recognized specific means of treatment of the various types of chronic occlusive arterial disease.

2. Rational treatment depends to a great extent on the results of a properly performed quantitative determination of the element of vasoconstriction in each extremity.

3. For patients with little or no vasoconstrictor element circulatory exercises and suction pressure therapy may be beneficial. Ligation of the main vein to the extremity has given worthwhile results in certain carefully selected cases.

4. For patients with a large or considerable element of vasoconstriction, conservative measures have been inadequate in the author's experience.

5. Lumbar ganglionectomy gives a greater, more continuous, and more persistent increase in circulation to the lower extremity with pronounced vasoconstriction element, than any other type of treatment. Preganglionic cervicothoracic sympathectomy gives comparable results in the upper extremity. The operations have a low mortality.

6. The vasodilatation following sympathectomy diminishes the likelihood of onset of thrombosis, and increases the collateral circulation, giving the greatest insurance against the serious complications of chronic occlusive arterial disease.

PANCREATIC EXTRACT (ENZYME-FREE) IN THE TREATMENT OF DIABETIC AND ARTERIOSCLEROTIC GANGRENE*

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IN spite of skillful insulin administration, gangrene of diabetic origin is still very common. Survey of statistical data for the last decade[1,2,13,15,16,17,18,19,21,24] shows variations in the incidence of gangrene from 3.1 to 25 per cent with a mean average of 8.5 per cent. Comparative statistics compiled by Kramer[16] in 1932, showed an average of 6.28 per cent.

These figures, however, refer merely to the *incidence* of gangrene among the diabetics. As the cause of death, diabetic gangrene has advanced from a rather humble status to a very prominent position. Two or three decades ago it was near the bottom of the list as a cause of death among diabetics; within the last decade it has moved up considerably, and in some clinics is now third on the list. My survey of statistical data on gangrene as cause of death in diabetes yields a mean average of 24.6 per cent. This closely agrees with the 20 to 30 per cent range quoted by Edelen.[8] Thus, as a threat to life in diabetics, gangrene looms with increasing menace.

Several authors, while calling attention to this increase, attribute it to the lengthened life-span of the diabetic since the advent of insulin—a life-span which, presumably, may now include the "arteriosclerotic decades." It is difficult to decide at present whether this increased life-span actually benefits the higher age group, or whether the increase is merely due to greater survival in the lower age brackets. The question is still an open one.

It must also be borne in mind that atherosclerosis and diabetes are inseparable. This may be an important contributory factor in the occurrence of gangrene.

Insulin with all its subsequent improvements did not substantially influence the mortality nor the morbidity of gangrene. Joslin states that fewer and fewer diabetics now die of diabetes; he regards deaths due to coma as absolutely avoidable. Yet when gangrene develops, the outlook for the gangrenous extremity is still hopeless in the opinion of most authors. Many stress prophylaxis; this having failed, radical amputation is mandatory in all cases of moist gangrene. Somewhat greater latitude, however, is allowed for dry gangrene where more conservative treatment may be instituted. Some authors advise hot air, electric cradle and suction apparatus, as well as iodides, acetylcholine, etc. I shall deal later with some aspects of these conservative methods.

For a number of years we have obtained very favorable results by treating cases of diabetic and arteriosclerotic gangrene with various enzyme-free pancreatic extracts prepared and standardized according to our previous publications.[26,27,28,31] Some of our methods were reported before the International Physiological Congresses, in Rome in 1932,[31] and in Leningrad in 1935.[28]

The early rationale for using this substance was based mainly on the work of Frey and Kraut,[10] and of Vaquez and his co-workers,[25] who showed that the pancreas contains a vasodilator substance. My colleagues and I have since discovered and reported[26,27,28,31,32] that it possesses many other pharmacologic properties:

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(A) We believe it to be a parasympathetic stimulant—perhaps a cholinergic hormone—for the following reasons:

1. It neutralizes the rise in blood pressure produced by epinephrine.
2. Topical application to the bullfrog eye constricts the pupil and neutralizes the dilator effect of epinephrine.
3. It increases peristalsis.

(B) This substance aids in fat metabolism, i.e., it lowers blood cholesterol and phospholipids after parenteral administration.

(C) In depancreatized dogs it prevents fatty degeneration of the liver and prolongs the life of the animal, as reported in Leningrad in 1935.[28]

(D) It causes appearance or increase in human urine of a substance related to choline, which is detected, like choline, by adding a solution of bismuth iodide in nitric acid to the urine.*

After injection of pancreatic extract, the quantity of brick red precipitate increases over a period of a few hours. In our experience there is a relationship between the quantitative appearance of this substance and actual clinical results.

(E) Our clinical impressions suggest that pancreatic extract prevents certain trophic changes.

We shall briefly summarize here a series of 100 cases treated with pancreatic extracts. This series comprises sixty cases of diabetic-atherosclerotic gangrene and forty cases of non-diabetic-atherosclerotic gangrene. The age range of the patients was from 44 to 78 years.

We divided all our diabetic cases treated with pancreatic extracts into two groups. The first consisted of those with beginning dry gangrene, darkening of toes or fingers or both, and sloughs no larger than 1.5 cm. in diameter and approximately 0.25 cm. in depth if ulcerated. (Figs. 1 and 2A.) Moist spots were often present. This group comprised thirty-three cases. Of these, twenty-nine (88 per cent) were healed completely; two had amputations; other cases could not be followed up. This type of case responds best to pancreatic extract therapy.

The second group of diabetics comprised twenty-seven cases of more extensive gangrene. (Fig. 3A.) Here moisture was present in most cases. The results, while not so spectacular as in the first group, were, nevertheless, highly gratifying. Seventeen (63 per cent) were healed completely, with a maximum loss of one to three toes or loss of tissue to the extent of the necroses. Only seven came to amputation. It must be stated that of these seven, two coöperated poorly, while the other five were extremely toxic with the infection so far advanced that there could be no hope of recovery. In this latter group there were three deaths—one due to cerebral thrombosis and two due to pneumonia. Three cases could not be followed.

The only cases accepted for treatment with pancreatic extract were those not exceeding the degree of pathology shown in Figure 3A.

The group of forty non-diabetic-arteriosclerotic (Fig. 4), gangrene cases treated with pancreatic extract showed the following results: Complete recovery was obtained in twenty-seven (67.5 per cent), together with a markedly increased walking capacity. Four cases could not be followed. Amputation was necessary in nine, of whom five survived, two died of pneumonia, one of cerebral embolism, and one of progressive heart failure.

Some of the cases had been under observation for several years. Whenever the patients complained again of pains, leg cramps, and difficulty in walking, the treatment with pancreatic extract was repeated.

* The test is as follows: Five drops of this reagent are added to 2 c.c. of urine in a small test tube. The tube is centrifuged for thirty seconds at a high speed or allowed to stand for six to twenty-four hours. The presence of a brick red precipitate adhering to the bottom of the tube indicates the presence of this substance in the urine. The quantity of brick-red precipitate gives an indication of the amount of this substance in the urine.

The following are a few illustrative cases:

Case 1. H. T., age 46 years, a white male clerk, complained of constant numbness and tingling of his feet, marked limitation of effort, and intermittent claudication. He had been taking insulin since 1934. In the winter of 1935–36, he was treated for "soreness" of the middle toe of the right foot, which responded to rest in bed (seven months), diet, and higher insulin dosage. He first came to us in June 1936. He had been on a strict diet with 35 units of insulin daily.

Pulsations in both the dorsalis pedis and the posterior tibial arteries were absent. The middle toe of the right foot presented a purple red area and there was a serous ooze from a very small dorsal opening. Pachon oscillometric readings revealed zero oscillations below the left knee and less than one quarter below the right knee. The urine was negative for sugar. The blood sugar level was 96 mg. per 100 c.c.

The diabetes was obviously under control and no change in the patient's régime was made except for triweekly intramuscular injections of 2 c.c. of pancreatic hormone (Grant). His toe symptoms decreased considerably in severity; pancreatic hormone administration was consequently reduced to biweekly injections. Improvement continued, and soon he was no longer "foot conscious."

On March 29, 1937, he returned following a slight injury to the middle toe of right foot, which he incurred while mowing the lawn. The toe became black and began to ooze profusely.

Fig. 1. Typical dry gangrene lesion.

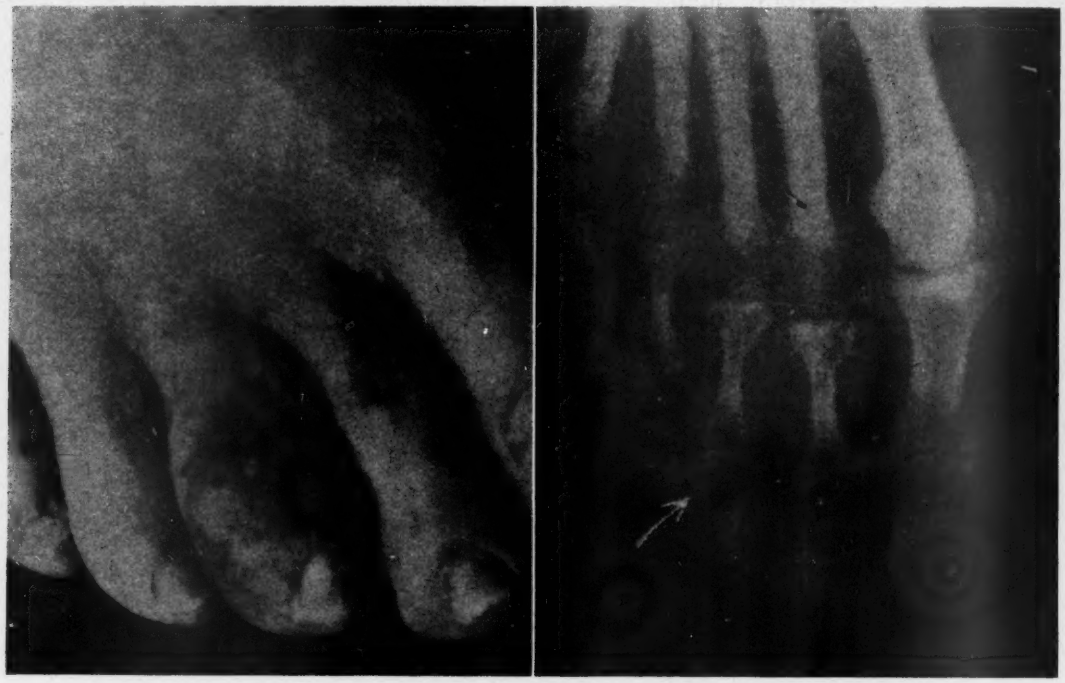
(Fig. 2A.) Examination elicited crepitation in the affected toe; osteomyelitis and fracture of the terminal phalanx were suspected and confirmed by *x*-ray. (Fig. 2B.) The patient was admitted to Temple University Hospital where Dr. Worth B. Forman performed a phalangectomy. Recovery was uneventful and the healing was complete. (Fig. 2C.) Insulin dosage was decreased. Walking capacity was greatly improved.

This case illustrates several interesting facts: (1) the importance of *x*-ray study in cases of diabetic gangrene for possible osteomyelitis; (2) an uneventful recovery following phalangectomy without further surgery; (3) the possibility of reducing the insulin dosage during the course of treatment with pancreatic extract.

Case 11. Mrs. K. C., 65 years old, was admitted to Bridgeton Hospital, on the Service of Dr. Leslie Myatt, in February 1937. There was advanced gangrene of the second and third toes on the left foot with discoloration and bleeding. Generalized arteriosclerosis was present. The patient was in pain and toxic, and her temperature was elevated. The left foot was bluish and discolored—a patchy type of discoloration with wet, moist, "smelly"

gangrene involving the second and third toes, with large patches, sloughing in character, on the dorsal as well as plantar surfaces of the foot. The skin of the large toe was markedly discolored and blistered. (Fig. 3A.) Her diabetes was under control.

Pancreatic hormone (Grant) was administered in doses of 2 c.c. twice daily for three weeks, and then every other day. The response was beyond expectations. A photograph of the same case three months later (6/10/37) is shown in Figure 3B. The patient does all her housework, can walk one-half mile daily without difficulty, and her insulin dosage has been reduced from 30 units daily upon admission, to 10 units daily.



A B

FIG. 2. Case 1. A, gangrene of middle right toe. B, osteomyelitis and fracture of the terminal phalanx of the middle toe following injury.

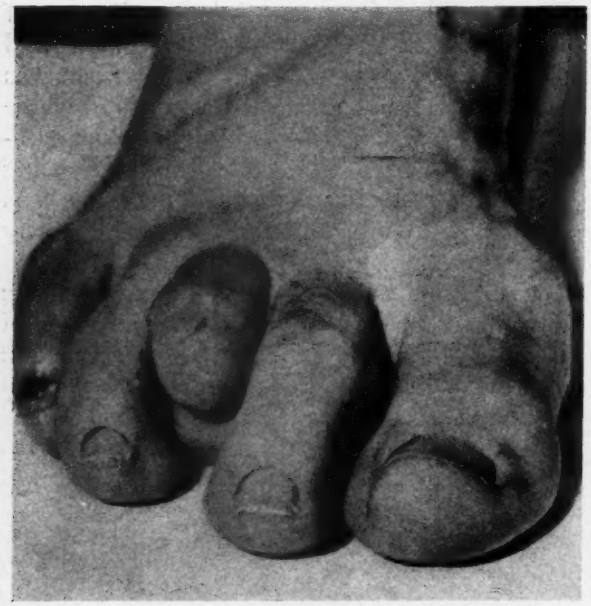


FIG. 2C. Case 1, six weeks after phalangectomy.

This is a borderline case, in which the prognosis must be guarded. Though our greatest number of failures has been among this type of case, a result such as this is very encouraging.

CASE III. Mrs. L. P., 74 years old, was seen in consultation with Dr. George A. McGinnis of Norristown, Pa. on September 13, 1936. The following is an abstract of the case by Dr. McGinnis:

"Patient suffered from arteriosclerotic senile, non-diabetic gangrene. She had severe pain in her left foot and right hand; the left great toe and the right thumb were black to the first joint. There was no radial pulse, and the posterior and anterior tibial pulses were also absent. Pancreatic extract (Wolffe), 2 c.c., was given intramuscularly daily for twelve days, then every other day. The pain in the foot and hand subsided after the first twelve days and their appearance became more normal; there

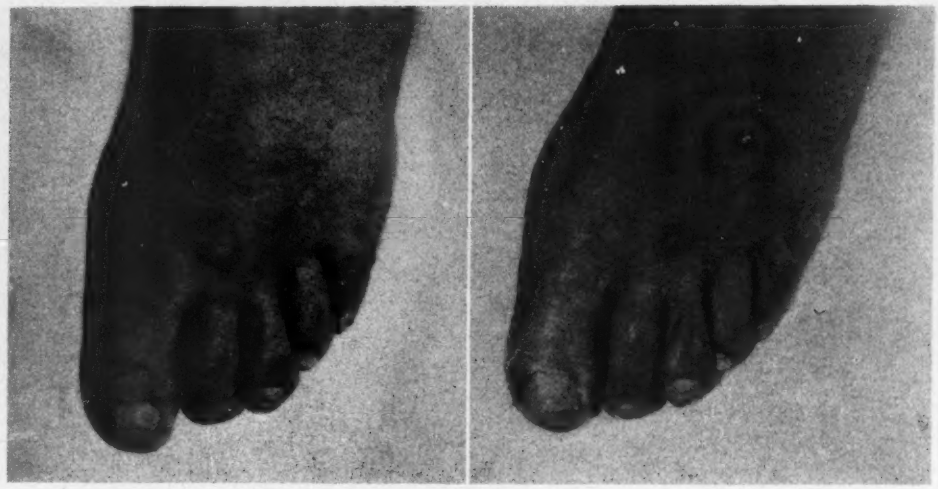
A B

Fig. 3. Case II. A, advanced gangrene of second and third toes of the left foot. B, three months later. Notice reappearance of the matrix.

A B

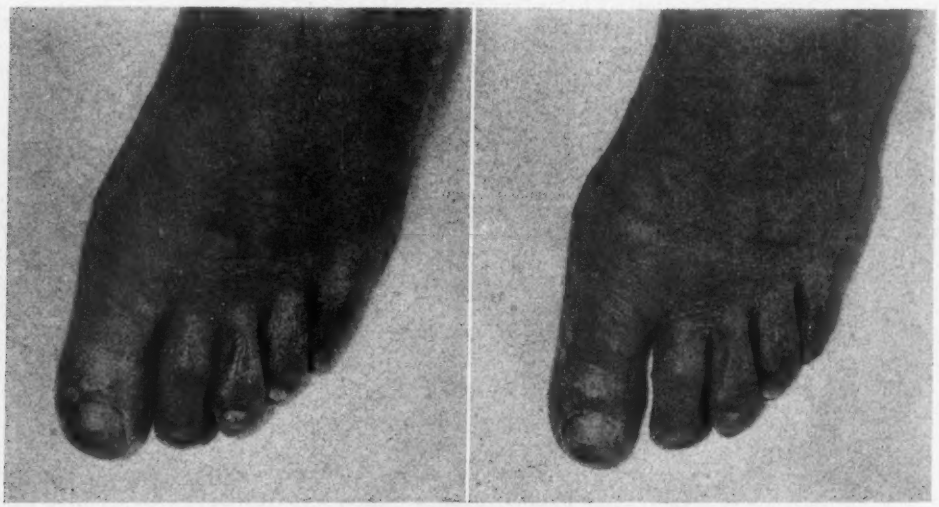
Fig. 4. A, non-diabetic arteriosclerotic gangrene. B, after treatment with pancreatic extract.

seemed to be a gradual return of circulation. Injections were continued (2 c.c. twice weekly) for twelve more weeks. No other medication



A B

FIG. 5. Case VII. A, before treatment. Anterior half of foot red, swollen and very painful. Small gangrenous area at edge of nail of first toe. Blood pressure 212/110. B, after ten days' treatment. No pain during week. Necrotic area healing. Less edema. Blood pressure 160/95.



A B

FIG. 6. Case VII. A, after three weeks' treatment. Necrotic area completely healed. Much less edema and redness. No pain or discomfort. Blood pressure 150/92. B, after one month of treatment. There is still some redness of toes when foot is dependent, but edema is much less marked. Blood pressure 144/92.

except sedatives and laxatives was given. She made a perfect recovery. Color was restored to both hand and foot; the right hand was somewhat claw-like in appearance due to arthritic changes in the joints; this remained unaffected. The result following the use of pancreatic extract in this case was spectacular."

CASE IV. J. H., a white male of 57 years, was treated by Dr. C. P. Lummis, of Salem, N. J. In 1934 he very gradually developed the usual symptoms of obliterative arteritis. He had cyanosis and coldness of both feet and ankles, most marked in the left foot. He also had slight pain and moderate claudication. Following a severe illness (rupture of gastric ulcer and operation) in March 1935, his arteritis became much worse. Rather severe pains developed, requiring drugs for relief; there was an absence of the posterior tibial and dorsalis pedis pulses in both feet and marked rubor (grade 3) was noted.

He was started on pancreatic tissue extract (Sharp & Dohme) in April 1935 with a dose gradually increased to 3 c.c. every three days. Pancreatic extract has been continued in 3 c.c. doses every three or four days and he is greatly improved. The ulcer on his toe is completely

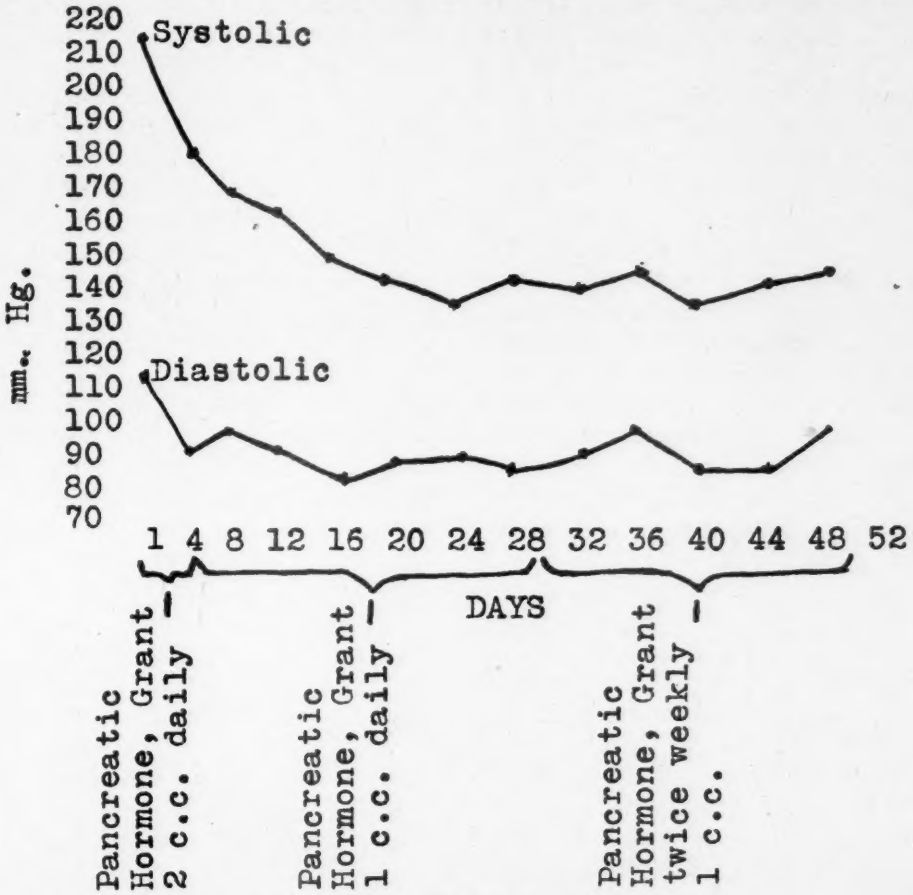


Fig. 7. Case vii. Blood pressure chart.

In about one month, marked improvement took place and he was able partly to resume work. All the symptoms gradually improved. Rubor of grade 1 was still present; but there was no pain. Claudication was present, but was much improved, he can walk about 4 blocks without pain. He continued with pancreatic tissue extract until August 1935, when he discontinued treatment against advice. In November 1935 he developed severe pain, rubor grade 3, and very dark blue, almost black, discoloration of the second and third toes of his right foot. An ulcerated area developed at the distal extremity of the second toe and it was thought amputation might be necessary.

Pancreatic extract administration was again started and the dose rapidly increased until 3 c.c. was given every third day. In about four weeks, marked improvement was noted, and in December 1935, he resumed part-time work. healed; the pain has entirely gone; rubor grade 1 is present and he can now walk about four blocks without claudication. No other medical treatment was given; but he has used Buerger's exercises and contrast baths.

Case v. Mrs. J. Y., white, 62 years old, was admitted to the Wilmington General Hospital, service of Dr. J. M. Barsky. She had had diabetes for four years. Two days before admission, she noticed soreness in the feet, a tired feeling, weakness, headache, and feeling of complete exhaustion, even though she did only the usual amount of housework. The patient was discharged with diabetes controlled, but returned six months later, with typical dark red blisters on the toes of the left foot. The blisters ruptured, leaving small gangrenous areas. Two weeks of bed rest and control of the diabetes failed to improve the appearance of the feet. Pancreatic hormone was then administered, and resulted in com-

plete healing. There was a recurrence about nine months later. Pancreatic hormone was again administered, followed again by complete healing.

Case vi. G. K. R., male, white, aged 76, was admitted to the service of Dr. Barsky, in the Wilmington General Hospital, Wilmington, Delaware. The patient had diabetes of five years' standing, and took 30 units of insulin at the time of admission. He complained of pain and ulceration in the left foot and a purulent discharging sinus at the base of the left big toe. There was intermittent claudication of the left leg. On dependent position, the left leg became red and purple in color. *X*-ray showed a destructive bone process particularly marked in the distal half of the first metatarsal and the end of the first phalanx of the great toe. Treatment consisted of stabilization of the diabetes; and the administration of pancreatic extract. The patient was discharged completely healed.

Case vii. C. B., white male, 74 years of age, was treated by Dr. Clifford C. Baker of Vineland, New Jersey. His past medical history was essentially negative. Mild symptoms of hypertension had been present during the past two years, but otherwise his recent health had been good. For several weeks the patient had noticed some edema of the left foot and complained of a feeling of coldness and occasional numbness of the toes of the left foot. Several days before he began to have burning pain in the toes and the anterior half of the affected foot and noticed that in this region there was a marked redness which would disappear when the foot and leg were elevated. At the medial border of the nail of the first toe there appeared a small area of discoloration of the soft tissues and this gradually increased in size over the course of several days.

The patient was normally developed but slightly undernourished, although he appeared to be in good general health. The heart was slightly enlarged, with sounds of fair quality and regular rhythm. The pulse rate was 84 and the blood pressure 212/110. The peripheral vessels were somewhat sclerotic and beaded.

Several small varicosities were present on the left leg, the toes and the anterior half of the foot were markedly swollen and red, with the red portion becoming blanched when the leg was elevated. The dorsalis pedis and the posterior tibial pulsations could not be felt. At the medial edge of the nail of the first toe there was a small area of discoloration.

The urine was negative for sugar but showed a very faint trace of albumin.

A diagnosis of early arteriosclerotic gangrene was made.

A sterile dressing was applied to the necrotic area and the patient advised to continue with a moderate amount of walking. A diet of 1,100 calories containing carbohydrate 100 gm., protein 60 gm., and fat 50 gm., was ordered and the patient was asked to take ½ ounce spiritus frumenti b.i.d. The patient was given intramuscular injections of 2 c.c. of pancreatic hormone daily for the first four days and thereafter 1 c.c. daily.

By the fourth day of treatment the patient experienced marked relief of pain and the local necrosis on the first toe showed no signs of further increase in size. There was gradual improvement in the general appearance of the foot and in less than three weeks the necrotic area had completely healed. Blood pressure (systolic and diastolic) showed a gradual decrease as shown by the accompanying graph. After the first month the injections of pancreatic hormone were given twice weekly in 1 c.c. doses, rather than daily. Diet and other treatment was not changed. The patient continued to improve and his blood pressure averaged 145/95. Subjectively he felt in better health than he had for several months previous to his illness.

SUMMARY

Patients in my series of 100 cases summarized earlier in the article, seemed to do very well, presenting about 75 per cent of complete healing. Most of them were treated conservatively. It must be stressed that injections of pancreatic extract did not constitute the sole treatment in all the cases. The extract was administered in doses of from 1 to 3 c.c., either daily or on alternate days, depending on indications, *in addition* to an adequate diabetic regimen. Nor were other measures neglected, such as proper hygiene, asepsis, short wave diathermy, low fat diet, etc. Typical management of a case included:

1. Papaverine hydrochloride gr. ¼ Acetylsalicylic acid, gr. 5
   Every three hours for pain.
2. Keeping the extremity warm. Appropriate non-irritating dry dressings.

3. Low cholesterol diet and indicated amounts of carbohydrates. Insulin when indicated.
4. Spirit. frumenti ℥ ss, b.i.d.

The patients were encouraged to be up and about as soon as possible, in order to aid the utilization of carbohydrates and fats by increasing energy requirement.

Since there is an optimal temperature which is most favorable for healing, we felt that the electric cradle might prove injurious in many cases and we therefore did not encourage its use. Similar objections based on the degree of stimulation may be raised against the various types of positive and negative pressure apparatus and for this reason these were not used in our cases.

The usual diabetic management fails in many cases of gangrene, necessitating radical surgery. I attribute this to the lack in insulin of some substance present in the pancreatic extract (desympatone). In some cases insulin alone seems to disturb muscle physiology. This can be judged from the fact that many diabetics with angina pectoris have refused to take insulin or learned to be cautious about it, because anginal seizures were often precipitated following the administration of even small amounts.[34] On the other hand, when these patients are given insulin with pancreatic extract, their tolerance is restored.

This may be due to the fact that in many diabetics there is a disturbance both in the lipoid and carbohydrate metabolism, and the effect of insulin, which is directed against the carbohydrate disorder alone, tends to produce a metabolic disequilibrium between the lipoid-carbohydrate relationship. Further studies along these lines are being conducted by my associate, Dr. Digilio, and other members of our group.

The active substance present in the enzyme-free pancreatic extract, which is neither histamine nor choline, exerts a beneficial influence upon lipoid metabolism, as well as upon muscle metabolism in general. As a corollary to this, it may be that the combination of insulin, pancreatic extract and a diet low in fats, will prevent the early appearance of atherosclerosis in diabetes. In the event of the latter, it is possible to expect a decreased incidence of diabetic gangrene.

CONCLUSION

Pancreatic extract (enzyme-free) proved of great value as an additional therapeutic agent in the management of diabetic and arteriosclerotic gangrene. It not only produces an early arrest of pathologic processes, but seems to stimulate repair more rapidly and more completely than any other conservative method in my experience.

I wish here to express my gratitude for help and collaboration to Dr. Joseph M. Barsky of Wilmington; Dr. Leslie Myatt, Bridgeton, N. J.; Dr. I. Stallberg, Atlantic City; Dr. T. P. McConaghy, Camden; Dr. J. P. Giambolvo, Philadelphia; Dr. D. J. Donnelly, Philadelphia; Dr. A. S. Hyman, New York; Dr. C. P. Lummis, Salem, N. J.; Dr. V. A. Digilio, Philadelphia; Dr. J. Pescatore, Philadelphia; and Dr. J. C. Munch, Lansdowne, and Dr. Clifford C. Baker of Vineland N. J.

REFERENCES

1. Allan, Frank N. Diabetic gangrene. *S. Clin. North America*, 1936: 1701–1706, 1936.
2. Audier, M. M. Les gangrènes diabétiques. *Marseille méd.*, 72: 289–312, 1935.
3. Boulin, Raoul. Le traitement des gangrènes diabétiques. *Presse méd.*, 44: 179–180, 1936.
4. Brandaleone, H., Standard, S., and Ralli, E. P. Prophylactic foot treatment in patients with diabetes mellitus. *Ann. Surg.*, 105: 120–124, 1937.
5. Caizzone, G. Le gangrene diabetiche. *Rassegna intern. di clin. e terap.*, 17: 351–359, 1936.
6. Dillon, E., and Hitzrot, L. H. Nonsurgical treatment of diabetic gangrene and infections of lower extremities. *Pennsylvania M. J.*, 37: 321–323, 1934.
7. Digilio, V. A., and Wolffe, J. B. Enzyme free pancreatic tissue extract. *Med. Rec.*, Sept. 15, 1937.
8. Edelen, C. M. Diabetic gangrene. *Kentucky M. J.*, 35: 326, 1937.
9. Eliason, E. L., and Wright, V. W. M. Treatment of diabetic gangrene. *S. Clin. North America*, 1931: 1275–1293, 1931.
10. Frey and Kraut. *Ztschr. f. Biol.*, 84: 321–324, 1926.
11. Halford, A. C. F. Diabetic gangrene. *M. J. Australia*, 23: 121–122, 1936.

12. Harms, H. P., van Prohaska, J., and Dragstedt, L. R. The relation of pancreatic juice to pancreatic diabetes. *Am. J. Physiol.*, 117: 160–165, 1936.
13. John, H. J. Exacerbations of diabetes. *South, M. J.*, 29: 1091: 1099, 1936.
14. Jordan, W. R. Care of the feet in diabetes. *Virginia Med. Month.*, 63: 465–467, 1936.
15. Joslin, E. P. Treatment of Diabetes Mellitus. Philadelphia, 1937. Lea and Febiger. Sixth Edition.
16. Kramer, D. W. Diabetic gangrene: incidence and pathogenesis. An analysis of 58 cases among 1008 diabetics. *Am. J. M. Sc.*, 183: 503–514, 1932.
17. Lyon, D. M., and Murray Lyon, R. M. Causes of death amongst diabetics. *Lancet*, 2: 293–294, 1930.
18. McGee, L. C. A survey of 490 diabetic admissions to General Hospital. *Am. J. Digest. Dis. & Nutr.*, 3: 178–181, 1936.
19. Margolin, M. Diabetes mellitus; a statistical analysis of 120 cases treated at the outpatient department of the University of Nebraska. *Nebraska M. J.*, 21: 1–6, 1936.
20. Meyer, Otto. Eine neue Methode zur Behandlung der feuchten Gangrän und zur Verhütung hober Amputationen. *Münch. med. Wchnschr.*, 83: 1172–1173, 1936.
21. Murphy, F. D., and Moxon, G. F. Diabetes mellitus and its complications. An analysis of 827 cases. *Am. J. M. Sc.*, 182: 301–311, 1931.
22. Olmsted, W. H. Arteriosclerosis of the lower extremities in diabetes mellitus. *Internat. Clin.*, 1: 195–209, 1936.
23. Rathery, F., and Rudolf, M. Les maladies de la nutrition en 1936. *Paris. méd.*, 101: 1–17, 1936.
24. Sevringhaus, E. L. A study of 500 diabetics. *Am. J. M. Sc.*, 182: 311–319, 1931.
25. Vaquez, Giroux and Kisthinios. Angina pectoris; action of pancreatic extracts on treatment. *Presse méd.*, 37: 1277, 1929.
26. Wolffe, Findlay, and Dessen. Treatment of angina pectoris with a tissue vasodilator extract. Preliminary report. *Ann. Int. Med.*, 5: 625–642, 1931.
27. Wolffe, J. B. Therapy of tissue extract (desympatone). *Tr. Am. Therap. Soc.*, 1931: 31–43, 1931.
28. Wolffe, Munch, Rabinowitz and Digilio. Desympatone—a fraction of insulin-free pancreatic extract. Summary of communication. 15th International Physiological Congress in Leningrad-Moscow, August 1935.
29. Wolffe, J. B., and Digilio, V. A. Unpublished data.
30. Wolffe, J. B., and Digilio, V. A. Pancreatic extract (tissue extract). *J. Lab. & Clin. Med.*, Jan. 1937.
31. Wolffe, J. B., et al. Pancreatic hormones; extracted after the removal of insulin. Summaries of communications. 14th International Physiological Congress in Rome, 1932.
32. Wolffe, J. B. Angina pectoris; its treatment with insulin-free pancreatic extract (desympatone). *Med. World*, June 1933.
33. Munch, J. C., and Wolffe, J. B. The effect of Norit on the depressor constituent of tissue extract (desympatone). *Arch. internat. de pharmacodyn. et therap.*, 44: 4, 1933.
34. Hyman and Parsonnet. Insulin angina. *Ann. Int. Med.*, 4: 1247, 1931.

AN IMPROVED CESAREAN SECTION TECHNIQUE

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MUCH has been written recently on the increasing incidence of cesarean section with its accompanying high mortality due to hemorrhage and infection. The abnormal death rate, well over 60 per cent in 1876, induced Porro of Pavia to attempt to overcome the dangers by doing a supravaginal amputation of the uterus after the delivery of the child. However, the Porro operation did not lessen the maternal mortality.

The greatest dangers and complications of cesarean section had come from the uterine incision, which tended to produce hemorrhage and peritonitis, the latter from the seepage of lochia into the abdominal cavity. In 1882 Max Sanger successfully sutured the uterine wound with silver wire and silk. This improved the operation of cesarean section and lowered the death rate by some 20 per cent. Notwithstanding the improved aseptic technique, such complications as hemorrhage, infection, peritonitis, peritoneal adhesions and rupture of the uterus during subsequent labor, occured all too frequently. To overcome these complications low cervical section was revived and practiced in 1906 by Frank of Cologne, Germany, although when it had been performed a century before by Osiander and Joerg, it had met with little success.

The excellent work of Sellheim, Döderlein, and Latzko helped to bring the low cervical operation back into vogue, and by the writings of Beck, De Lee and, more recently, Phaneuf, this method was introduced on this continent.

Gottschalk of Berlin, in 1911, and Portes of Paris, in 1924, added a further point when they brought the uterus out of the abdomen (temporary exteriorization) in infected cases and kept it out until the infection was controlled. Then the uterus, which had partially or completely involuted, was returned to the abdomen or, if still infected, was removed.

Extreme conservatism is now advocated in the employment of cesarean section; it should be resorted to only in the unquestioned indications, such as contracted pelvis, cephalopelvic disproportions, tumors obstructing the pelvic outlet, stenosis of cervix, advanced heart disease or tuberculosis, in some cases placenta previa, etc., according to recent reports, most of which recommended a trial of labor up to two hours after the complete dilatation of the cervix. It is stated that many parturient women would deliver if left alone and given a trial of labor. But it is often this trial of labor that exhausts these women and has proved the turning point against them, thereby increasing the maternal mortality.

The trying ordeal which a difficult labor inflicts on women is not, I think, sufficiently appreciated. Excessive loss of blood, lacerated cervix, injuries to the bladder, bowel, vagina and perineum, retained parts of placenta and membranes, subsequent infection, septicemia, phlebitis, endometritis and endocervicitis are frequent causes of morbidity in women. These factors, in addition to the mental and physical pain of difficult labor make it worthwhile to attempt alleviation if this should be possible.

Few women are the same mentally or physically after a difficult confinement. The vaginal canal is often so torn, stretched and injured that proper marital relations have not only become less agreeable, but in many instances painful or even unbearable. Many marriages are harmed on this score alone. The large number of suspensions, plastic operations for prolapsus uteri,

repair of cervix or vagina, cystocele, rectocele, coaptation of widely separated recti, the increasing need for the application of radium to the cervix are testimony to the extent of obstetrical trauma. Pelvic adhesions caused by puerperal infections often necessitate later operation. Six hundred operations of this type were done at the Vancouver General Hospital in 1936. Carcinoma rarely occurs in a cervix that has never been dilated or torn by childbirth.

It is also true that few babies come unhurt through the birth canal during a difficult labor, especially if it is the first. The squeezing and compression even in normal cases, to say nothing of the abnormal ones, cannot but be undesirable. The old teaching that this process accumulates carbon dioxide in the blood stream to stimulate the respiratory center has now been exploded. Last year at the Vancouver General Hospital the fifty-seven stillbirths and thirty premature deaths were nearly all due to difficult labor. This mortality could be greatly reduced if not entirely eliminated by timely cesarean section.

Cesarean section is done because the abdominal delivery offers the best chances for mother and child and avoids a vaginal delivery which would be multilating to the mother and possibly fatal to the baby. Experience has taught me that cesarean section, especially the low operation, done before labor sets in, leaves little to be desired. I am not unmindful of the high mortality and morbidity of section in country-wide statistics. However, I think that both would have been negligible had section been done on properly indicated cases before labor had set in. With a technique which permits very little loss of blood and no amniotic spill, few complications appear. Infections and pulmonary embolism seldom arise under aseptic technique if operation is done early and active movements are begun soon after. The repeated examinations, the versions, use of forceps, and the exertion of a trial labor, however short, lower the patient's resistance, paving the way for infection and other complications.

Cesarean section has not reduced maternal mortality, because of delay in operating and the type of operation done. Severe labor and numerous unnecessary vaginal examinations are a bad prelude. Unjustifiable operations are done on eclamptic, nephritic and septic patients. In addition, one must emphasize that only qualified surgeons should undertake such procedures.

However, there is no doubt that cesarean section performed by the technique now in vogue entails a great loss of blood with an amniotic spill which all too frequently enters the abdominal cavity. Even in the hands of competent surgeons the hemorrhage is often considerable, while in the hands of the less experienced it is often so great that postoperative shock and complications produce a high mortality.

The technique reported here should assist not only the surgeon, but also the occasional operator. It prevents amniotic spill and blood loss from the uterine wall incision. Too often tremendous hemorrhage is caused by cutting across the larger vessels in opening the uterus, since these vessels are difficult to see in the gush of amniotic fluid.

TECHNIQUE

Make an incision through the skin, subcutaneous connective tissues and anterior sheath of the rectus muscle near its medial border from the umbilicus to the pubes. Free the rectus muscle from the mesial border of its sheath and retract it outward. Open the abdomen by making an incision through the transversalis fascia and peritoneum, being careful to avoid the urinary bladder (which was previously emptied with a catheter).

The anterior surface of the uterus is now exposed the full length of the incision. Laparotomy pads should be arranged around the abdominal opening. If the low cervical cesarean section is preferred to the classical, make a transverse incision across the uterine peritoneum about an

inch above the bladder reflection. Dissect the lower flap of the peritoneum with the bladder from the anterior surface of the uterus and cervix. Also dissect the upper transverse flap of the peritoneum from the anterior surface of the uterus for such a distance as the longitudinal incision requires. Place two Allis tacks on the uterine wall at the top of the intended incision and make a small quarter inch opening between them. Insert a suction tube through this opening into the uterine cavity and syphon off all the amniotic fluid into a large receptacle.

Remove the suction tube and insert through the aperture in the uterine wall two curved (DeMuth) cesarean forceps (Fig. 1) which have been specially designed for this purpose. Clamp the uterine wall gently but firmly and make a 7 inch incision between the clamps. Note that very little bleeding has occurred and that no amniotic fluid is present in the uterine cavity. Turn the cesarean forceps on their side; this converts the uterine opening into an oval through which the fetus, placenta and membranes can be easily removed. Lift the baby out carefully. Sever the umbilical cord between two clamps, and pass the baby over to an assistant. Inject 1 c.c. of pituitrin into the uterine wall. Wait a few minutes and then remove the placenta and membranes. If at this stage of the operation the removal of placenta and membranes is not hurried there will be much less bleeding from the placental site.

Next see to it that the cervix is open. If not, dilate it with two fingers. Remove the cesarean clamps. The opening in the uterine wall will contract to nearly half its original size as the remainder of the uterus has already contracted. Close the uterine wall opening with three layers of continuous suture of No. 2 chromic catgut. Reperitonealize the uterine suture line.

Remove all abdominal wall pads. Close the abdomen in three layers in the usual manner without drainage, making sure to coapt the widely separated recti muscles. Apply a postoperative abdominal elastic wound support. Upon the patient's return to her room, give 1,000 c.c. of 5 per cent glucose-saline solution every six hours for the first two days.

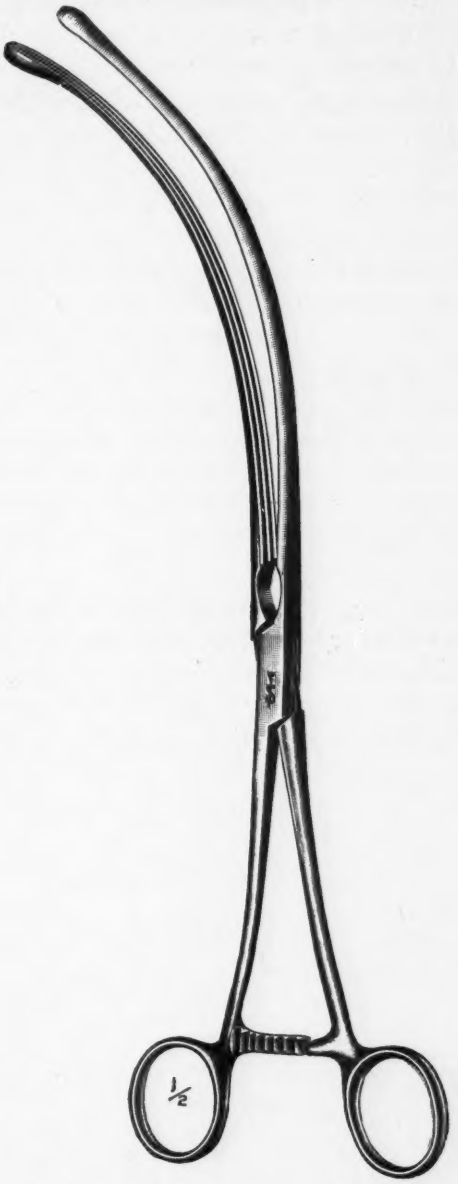

Fig. 1. DeMuth cesarean clamp.[1]

The amniotic spill, although it is physiologic to the amniotic cavity, is not so to the peritoneum. Most of the adhesions which occur following section are due to the exudative peritonitis caused by the spill of amniotic fluid or seepage of lochia through the uterine incision. Drawing off this fluid through a trocar causes the uterus to con-

[1] Made by Kny-Scheerer Corporation.

tract; with the removal of the child it contracts further. This permits one to lift up the contracting uterus in the abdomen so that an assistant can hold and gently compress it. It also enables the assistant to aid the contracting uterus by lateral pressure, and to compress the uterine vessels in each broad ligament if the need arises, while the surgeon sutures the wound in the uterus. Several pads are placed on the abdomen under a postoperative elastic support. This stimulates and maintains the uterus in contraction. It also restores the abdominal pressure so suddenly relieved.

I have had the good fortune not to have had a single maternal or fetal death from cesarean section in seventy-three cases operated upon over a period of seventeen years. No serious postoperative disturbances have been encountered beyond the usual effects incident to any major abdominal operation.

Of course, cesarean section is not to be done on every borderline patient by any physician who thinks himself capable. But there are few major abdominal operations the technique of which could be mastered more easily. With better suturing of the uterine wall, more timely operations, a technique which permits little loss of blood and amniotic fluid, and little or no infection, there is only a slight possibility of a weak uterine scar. There is, therefore, little risk of a rupture of the uterus in a subsequent pregnancy.

SUMMARY

1. Cesarean operation, when indicated, should be done before labor sets in.

2. Excessive vaginal examination prior to cesarean section is to be avoided.

3. A new technique is described with
   (*a*) Puncture of the uterus.
   (*b*) Syphoning off the amniotic fluid.
   (*c*) Insertion of specially designed cesarean clamps to prevent bleeding from the uterine wall.
   (*d*) Application of postoperative elastic wound support to maintain uterine contraction and restoration of the abdominal pressure, which the emptying of the uterus has relieved.

A MODIFIED CIRCUMCISION SUTURE TECHNIQUE

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THE classical method of suture in the operation of circumcision is to approximate the cut skin edge to the trimmed mucous membrane by interrupted sutures penetrating these layers. Occasionally, there results a "sawtooth" skin margin, the result of one or several sutures cutting through the skin. Such a necrosis is more apt to occur when too large a bite is included in the ligature.

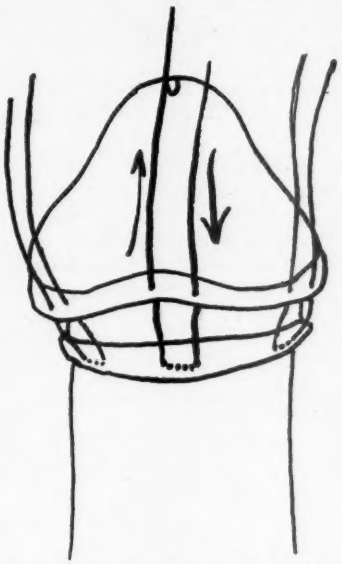

FIG. 1. Diagram demonstrating the subcuticular mattress suture going from without inward through the trimmed edge of the mucous membrane and taking a transverse subcuticular bite on the inside of the everted skin margin, finally being brought from within outward through the mucous membrane. The arrows show the direction of the suture at the frenum.

A perfect union of skin and mucous membrane may be obtained by using interrupted subcuticular mattress sutures, inserted first through the mucous membrane from without inward, then taking a subcuticular bite in the everted skin, the suture being passed transversely on the inside of the everted skin edge and back again through the mucous membrane from within outward. The sutures are

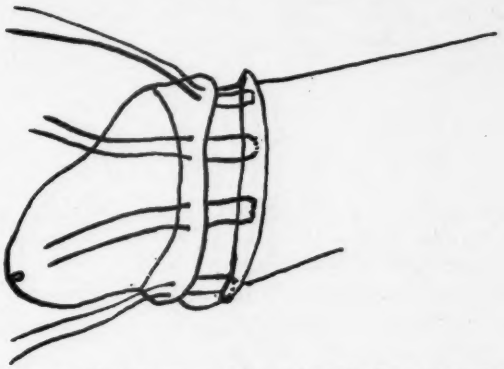

FIG. 2. Placement of the subcuticular mattress sutures at the midline dorsally, at the frenum and at equally spaced points on the lateral aspect.

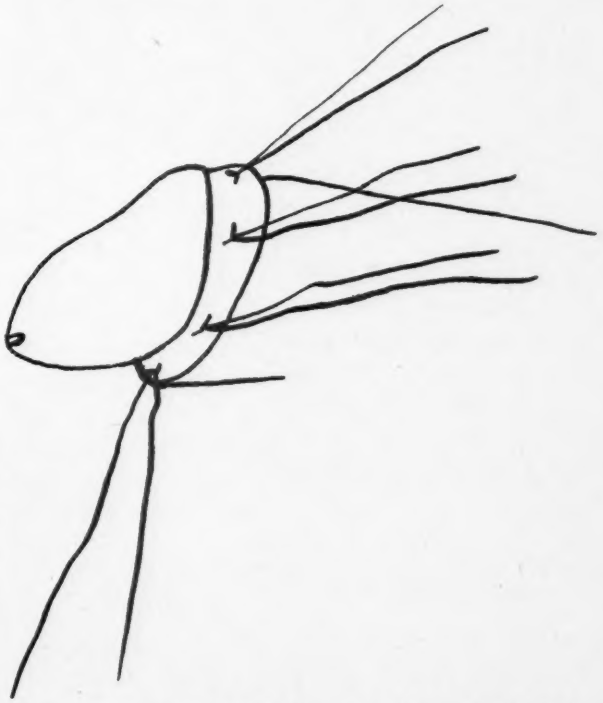

FIG. 3. Sutures tied and the ends left long to be tied over a piece of vaseline gauze.

placed at the frenum and dorsal aspects, then used as tractors until two such sutures are evenly placed on each side of the midline. The ends are tied and left long, to be tied again over a strip of vaseline gauze, which, when separating in a week or ten days, leaves an intact skin margin united to the mucous membrane.

By placing the sutures on the inside of the cut skin margin and not bringing the loop through the entire thickness of skin, one secures a fine cosmetic appearance, which requires a minimum of postoperative attention.

REFERENCES

Lanman, Thomas H. Indications and contraindications for circumcision in children. *Boston Med. & S. J.*, 190: 628–630 (April) 1924.

Cogswell, H. D. A safe technique for circumcision. *J. Indiana M. A.*, 28: 371–372.

Van Auken, William B. D. Infant circumcision. *New York State J. Med.*, 29: 82 (Jan. 15) 1929.

Bandler, Clarence G. Circumcision. *Am. J. Surg.* 6: 455–457 (April) 1929.

Walker, W. W. Electrosurgical circumcision. *Am. J. Surg.*, 6: 103–105 (July) 1929.

Rauschkolb, John E. Circumcision, its value in the treatment for chancroidal lesions of the male genitalia. *Arch. Dermat. & Syphil.*, 21: 251–256, 1930.

Canright, Cyril M. A simple circumcision operative procedure. *China M. J.*, 45: 152–153, 1931.

Harris, Hyman H. A new instrument for the simplification of circumcision. *M. J. & Rec.*, 135: 195–196 (Feb. 17) 1932.

Bettman, Adalbert G. An exact technic for circumcision. *West. J. Surg., Obst., & Gynec.*, 41: 220–221 (April) 1933.

Friedman, Alexander, A modified method of circumcision. *Urol. & Cutan. Rev.*, 38: 319–320 (May) 1934.

Bertwistle, A. P. Juvenile circumcision. Clinical and laboratory notes. *Lancet.*, 1: 85–86 (Jan. 12) 1935.

Harris, H. H. Instruments and technical methods. *Med. Rec.*, 140: 441–443 (Oct. 17) 1934.

Yellen, Hiram S. Bloodless circumcision of the newborn. *Am. J. Obst. & Gynec.*, 30: 146–147 (July) 1935.

TOTAL THYROIDECTOMY IN THE TREATMENT OF ANGINA PECTORIS

LATE RESULTS IN FOURTEEN CASES

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A GREAT number of total thyroidectomies have been done for patients suffering from angina pectoris or congestive heart failure since the introduction of this plan by Blumgart, Levine and Berlin. Sufficient time has now elapsed for the immediate results to be recorded. The primary problem is really a medical one, for only by careful study and selection of cases can the best ultimate results be obtained. We wish to add to the literature a report of our experiences with fourteen total thyroidectomies which were done for angina pectoris.

Each patient in the series had been given every advantage of medical management and had reached the state of invalidism. Each patient was carefully watched and studied so that not only the physical condition but also the cardiac and renal status was known. All had renal functions within normal limits. There was evidence of coronary sclerosis in all the cases and in one there was evidence of two small healed infarcts. The presence of a healed infarct has not been considered a contraindication to surgery.

The basal metabolic reading is very important, since it is not advisable to recommend total ablation if the rate is below minus fifteen. In this series the metabolic readings were all within normal limits. The anginal syndrome may be improved by elevating the metabolism in some of the eases with a low basal rate and a low blood pressure. The mechanism is an improvement in the coronary circulation.

We believe that the lessening of adrenal effect is responsible for the dramatic relief of pain in the angina pectoris cases, and a separate explanation of the results obtained in decompensated hearts must rest in the lowered metabolic demand, a limit which the damaged heart can supply. The lowering of the basal metabolic level is not an immediate phenomenon, but occurs about four to six weeks after the total ablation has been done.

The patients have been prepared by being placed in the hospital for two or three days previous to operation in order that they may become adapted to the surroundings. A sedative is given the night before and the morning of the operation. The surgery has been done by one of us (J. R. P.). The operations have been performed under local anesthetic supplemented by a little ethylene gas; in two cases the operation was done entirely under local anesthesia. The operation is not difficult and can be done in forty-five minutes to one hour. Every particle of the gland must be removed; otherwise there will be a regeneration of the remaining part and the temporary benefit will be lost. In addition, the recurrent laryngeal nerves must not be injured. However, the anatomic relation of these nerves has been so well worked out that this danger is minimal. There has been no cord paralysis in this series. The parathyroids, as a usual thing, are not greatly endangered; at least one has been demonstrated in every case. There was a transient parathyroid tetany in one case, which was easily controlled by calcium, cod liver oil and parathormone.

All the patients were operated on more than eighteen months ago, the first one

on April 12, 1934. There were nine men and five women in the series, their ages varying between 40 and 70 years.

These patients stand total removal very well, the general operative risk being between 5 and 10 per cent. There were two operative deaths in the series. The first occurred in a man, aged 70, who had a marked coronary sclerosis and had had two previous attacks of occlusion. His death was due to an acute occlusion, as shown at post-mortem examination. The second was in a man, aged 56, whose death was the result of a cerebral embolus from aortic arteriosclerotic ulcerations.

There have been seven excellent results and two cases with good results. Five patients are living over two years after operation. One individual had excellent results for one year, but has had two attacks of coronary occlusion since that time. Another died six weeks after operation of coronary occlusion. Still another died seventeen months after operation of coronary occlusion, though he had had fair results before his death.

Since surgical myxedema does not begin to manifest itself until four to six weeks after the whole thyroid is removed, there is no need for thyroid extract until that time. These patients take one tenth grain of active thyroid substance two or three times each day, which overcomes the greater portion, but not all the myxedema. One patient, although with a well marked myxedema, has had no distressing symptoms and consequently takes no thyroid extract.

Two patients have had very interesting experiences following total thyroidectomy. The first, a man who two years ago had a total removal for severe angina, about six weeks ago presented himself with a ruptured gangrenous appendix. He was operated on for this and had a very easy postoperative convalescence. The second, a woman who twenty-one months ago had a total removal for congestive failure with angina, has since conceived and carried the pregnancy to term without decompensation or pain. Her baby is now five months old and is perfectly normal.

Name	Age	Occupation	Date of Operation	Result
M. L. R.....	44	Clothier	4-12-34	Excellent.
H. C. H.....	46	Merchant	5-26-34	Good.
L. T. P.....	49	Contractor	5-28-34	Good—died 12-10-35, coronary occlusion, 17 months after operation.
A. M.....	51	Merchant	6-2-34	Excellent.
J. K.....	70	Ranchman	6-25-34	Died immediately after operation, coronary occlusion.
W. H.....	50	Theater	8-17-34	Excellent.
Mrs. C. A. P.	40	Housewife	10-9-34	Fair—excellent for one year, two attacks since.
N. T.....	50	Farmer	1-21-35	Relief for six weeks, death due to coronary occlusion.
Mrs. L. H....	48	Housewife	8-19-35	Good.
Mrs. M. B...	35	Housewife	9-30-35	Excellent.
Mrs. B. E. G.	25	Housewife	9-30-35	Excellent.
Mrs. E. F....	59	Housewife	10-15-35	Excellent.
J. C. N.....	45	Plumber	10-23-35	Excellent.
E. K. N.....	56	Ranchman	2-5-36	Died, cerebral embolus.

Not one in our series feels that he or she is cured. All of them live well within their pain range, yet each one is better and would gladly repeat the measure if necessary. They are all rehabilitated cardiac invalids. The present level of improved status fully justifies the use of total ablation of the thyroid gland in properly selected cases of angina pectoris.

SUMMARY

A series of fourteen patients, who had had total thyroidectomies at least two years previously, is reported. All of these patients were suffering from angina pectoris of the most severe form. All showed some degree of coronary sclerosis and several presented definite evidence of cardiac infarction.

We feel, from the evidence presented, that while none of these patients may be considered cured, the present level of improved status fully justifies the use of total ablation of the thyroid gland in properly selected cases of angina pectoris.

MORPHINE AS A FACTOR IN POSTOPERATIVE VOMITING

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AUTHORITIES generally agree that in some people morphine may cause nausea and vomiting, but the frequency of these symptoms is not so generally appreciated. Postoperative vomiting is commonly ascribed to the anesthetic, although, aside from the anesthetic, a preoperative hypodermic containing morphine is given and a surgical operation is performed. The ensuing vomiting may be due to any one or more of these procedures. Ordinarily it is not definitely determined which of them is the important factor.

In order to test out the morphine factor, this drug was given the night before operation to 200 consecutive surgical patients at the Immanuel Hospital. In this way the effects of the drug were determined and the factors of anesthetic and operation were eliminated. In a few of the cases the morphine was given hypodermically. However, as a matter of convenience, in most of the cases it was given orally (gr. ¼) with sodium bicarbonate in a capsule. Sollman has stated: "Morphine tends to produce nausea and vomiting and thus to disturb digestion. The effect is independent of the mode of administration, the action being central."

If the patient slept well and had no untoward symptoms, we felt that no unusual susceptibility to the opiate existed. However, if the patient developed nausea, vomiting, headache, or marked restlessness during the night, idiosyncrasy was considered to be present and some other opiate was substituted in the preoperative hypodermic. This series naturally did not include emergency cases where time did not permit the above procedure to be followed.

In cases of morphine idiosyncrasy codeine was usually used as a substitute, as this narcotic was usually better tolerated. The only objection to the routine use of codeine as a pre- and postoperative narcotic was that larger and more frequent doses were required to give the same analgesic narcotic action. The dose of codeine usually used in the preoperative hypodermic was 1 gr.

The following table illustrates the results obtained:

	Number	Percentage
Cases studied	200	
Morphine idiosyncrasies	25	12.5
Postoperative vomiting in non-sensitive patients	...	36.5
Anesthesia used		
Avertin-ether	...	74.5
Nitrous oxide-ether	...	11.0
Spinal	...	10.5
Miscellaneous	...	4.0

Morphine idiosyncrasy thus existed in 12.5 per cent of 200 consecutive surgical cases.

When morphine idiosyncrasy is not previously tested, it is a common practice to give morphine to patients who are quite uncomfortable with vomiting. In these cases a vicious circle is produced and vomiting continues. This unfortunate mistake may be prevented by the method described above.

CONCLUSIONS

Morphine is a much more frequent cause of postoperative vomiting than is generally thought.

It is suggested that, if morphine is to be used, a preliminary dose be given the evening before operation to test the patient for idiosyncrasy.

In case of idiosyncrasy to this drug it is advisable to substitute some other sedative before and after operation.

CASE REPORTS

A CASE OF PERIOSTEAL SARCOMA OF THE HUMERUS TREATED BY RESECTING, BOILING AND REPLANTING THE BONE*

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IN a paper published in 1936,[1] I described very briefly a case of osteogenic sarcoma of the humerus treated by resecting, boiling and replanting the bone. The bone was boiled in order to kill the tumor tissue, and replanted so that its calcium framework would support the soft tissues until new bone had developed. As the old bone had the most suitable shape and structure, it was preferable to use it for support instead of, for example, prepared bone such as os purum. The healing was primary. After the operation, there was no local recurrence, but roentgenograms two and one-half months later showed pulmonary metastasis which caused the death of the patient about fifteen and one-half months after the operation.

CASE REPORT

J. E. K., male, 16 years of age, was admitted July 30, 1935. The past history was negative except for measles during childhood. About Christmas time of 1934 the patient fell on the ice and hit his left shoulder. Although the immediate swelling was not great, at about the following Easter, April 1935, the left upper arm began to swell. The patient experienced no pain or tenderness, however, and no redness was observed. He noticed no weakness in his arm and had no difficulty in moving the shoulder joint. There was no loss of weight, no fatigue and no cough.

A series of Roentgen treatments had been given before admission for six days beginning May 31, and a second similar series beginning July 22.

At admission on July 30, 1935 the physical examination was entirely negative except that in the upper half of the left upper arm a spindle-shaped swelling was found. The skin was brownish-red in color. No distended veins were seen. Some increase of heat could be felt. On palpation the upper half of the arm was found to be firm and somewhat thickened, while on the anterior surface a somewhat more distinctly raised ridge was palpable. There was no crepitation or tenderness. The patient had good mobility in the shoulder joint, but could not abduct his arm completely upwards, lacking about fifteen degrees. The mobility of the arm was otherwise normal. There was some atrophy in the musculature of the upper arm, but the strength of the forearm and hand was fairly good. No enlarged lymph nodes were palpable in the axilla, nor in the supraclavicular or infraclavicular regions.

Examination of the blood showed the following: R.B.C. 4,400,000; W.B.C. 7,200; differential count: 77 per cent neutrophils, 5 per cent large lymphocytes, 15 per cent small lymphocytes, 1 per cent basophiles, 2 per cent monocytes.

X-ray examination disclosed an osteogenic sarcoma of the upper half of the left humerus. (Fig. 1A.) The chest plate showed no metastases.

On August 8, 1935, surgical resection, boiling and replantation of humerus together with implantation of os purum were performed. Under ether anesthesia an incision was made in the sulcus bicipitalis lateralis. The soft tissues were divided down to the periosteum and the latter was freed up over a wide area.

* Translated from the Swedish by Clifford C. Franseen, M.D., Boston, Mass.

The lower part of the shaft of the humerus was covered with layers of periosteal new bone, but no tumor masses were visible. An osteotomy was done by making multiple drill holes at the same level. By blunt subperiosteal dissection the proximal portion of the humerus was then freed up to the shoulder joint and removed. The upper third of the humerus was found to be enlarged by transparent, myxomatous masses which appeared to be quite well delimited. The bone was carefully cleared of these masses. Multiple holes were bored in the bone; and it was then boiled for ten or fifteen minutes in physiologic salt solution, and replanted with an os purum peg inserted in the distal end. The proximal end of the distal portion of the humerus was pushed onto the peg until a good position was obtained. (Fig. 1B.) The wound was closed without drainage. A fenestrated circular plaster cast was placed about the thorax, upper arm, forearm, and hand. The wound healed by first intention.

The pathologic diagnosis of telangiectatic osteogenic sarcoma was made by Dr. O. Reuterwall of Radiumhemmet, Stockholm.

A B C

Fig. 1. Roentgenograms of the left upper arm (frontal views). A, before operation. B, twenty-eight days, and C, 206 days after operation. The last picture shows a fracture at the junction of the upper and middle thirds of the humerus.

By September 12, 1935, the region operated upon appeared satisfactory. The patient could move the shoulder joint slightly, no crepitation could be elicited, and the swelling had receded. The plaster cast was then cut to enable the patient to move the entire arm. On October 3, the plaster cast was discarded. The strength of the arm was very good, and the patient could raise it above the horizontal plane.

On October 24, the musculature of the left arm appeared the same as that of the right except for a somewhat atrophic deltoid muscle. The muscle was strong enough so that a dynamometer test showed: right 22 Kg., left

14 to 16 Kg. A roentgenogram of the chest showed a shadow at the base of the right lung, rather rounded and about the size of a hazel

Fig. 2. Roentgenogram of the left humerus after post-mortem excision.

nut. The general condition was good, however, and the patient had gained 10 Kg. in weight There were no local signs of recurrence.

At examination on December 29, the patient felt well, but the left upper arm was found to be greatly shortened. There was a fracture of the left humerus, (Fig. 1c), although the patient was not aware that he had broken his arm, and no pain was elicited either on palpation or on movement.

On January 28, 1936, the general condition was good. The sedimentation rate was 10 mm. in 1 hour. A roentgenogram showed that the pulmonary metastasis had increased in size. The patient's general condition then began to suffer and he started to lose weight. The sedimentation rate increased to 35 mm. The lung metastasis grew larger; the patient became increasingly troubled by cough, and on November 26, 1936 died quietly at home. The parents reported that during the last month of his life he had had increasing difficulty in breathing but no pain.

Autopsy was not permitted, but consent was obtained for the removal of the bone of the left upper arm. (Fig. 2.) The tissue around the bone was entirely healthy and no signs of local recurrence had appeared.

Histologically this tumor was of an unusual type. A piece of the tumor tissue removed at operation from the surface of the humerus for histologic examination showed a peculiar type of myxomatous, chondro- and osteogenic sarcoma. (Fig. 3.) Wide vessels, occasionally arranged in hemangioma-like nodules, were found in the tumor tissue. (Fig. 4.) The borderline between the tumor and normal tissue could be studied in a few places, and no invasive growth was found. The margin showed only connective tissue, poor in cells. The relation between this tumor and its surroundings was, therefore, not that of an ordinary sarcoma.

In the post-mortem specimen, a few islands of tumor tissue were found in the humerus, but these islands appeared to be dead. No homogeneous tumor mass was found. The absence of local recurrence was most likely due to the unusually good delimitation of the tumor. It appeared that the greater part of the original tumor must have been located on the surface of the humerus, and for this reason I feel that it is most correct to speak of it as a periosteal sarcoma. It is unfortunate that we were unable to examine the histologic structure of the metastasis in the lung.

It appeared, also, from the microscopic section of the post-mortem specimen that the bone formation around the replanted humerus was scanty. Despite the slow resorption, the fracture probably occurred because the bone was weakened through the multiple perforations. The implantation of os purum would perhaps have given better results, with respect to both bone formation and structural strength.

CONCLUSIONS

It is hardly possible to draw any conclusions from this case regarding the

value of the method for the treatment of osteogenic sarcoma. However, it is clear that operation should be performed as early as possible. In this case, two months were lost in pre-operative Roentgen therapy which, in the light of later developments, was probably unfortunate.

This case is primarily of theoretical interest. It shows that it is possible to replant tumor-containing, boiled autoplastic material and obtain primary healing.

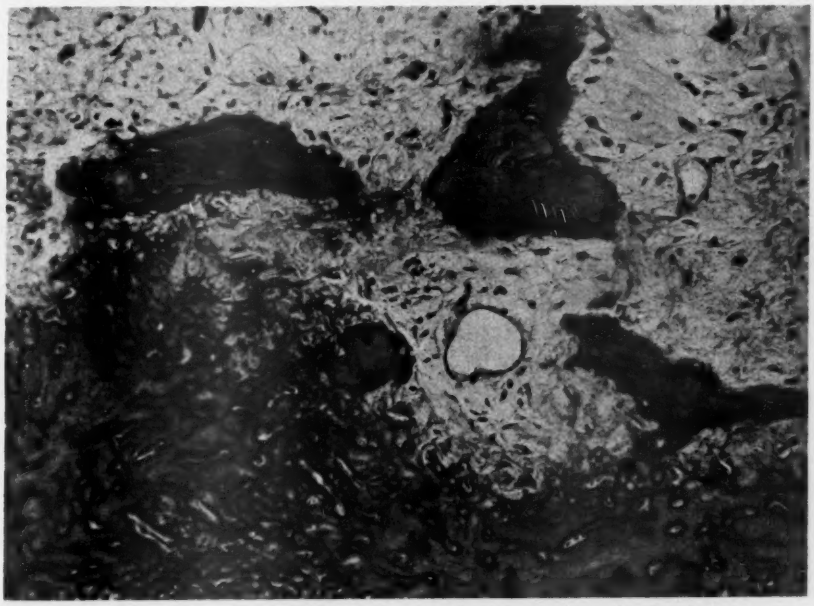

Fig. 3. Osteogenic sarcoma with wide vessels. Photomicrograph of the tumor obtained at operation. (× 180.) Hematoxylin-eosin stain.

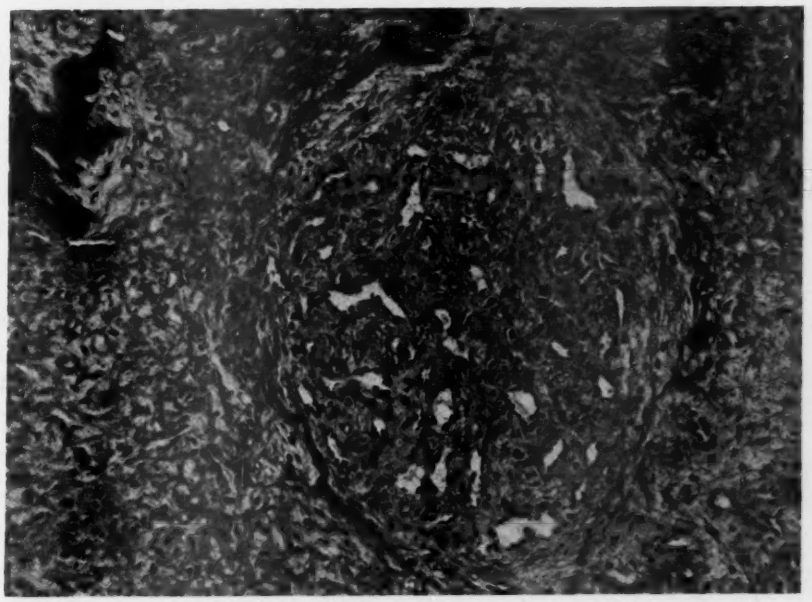

Fig. 4. Angioma-like nodule in the tumor tissue removed at operation. Hematoxylin-eosin and van Giesen stain.

REFERENCE

1. Orell, Svante. Knochentransplantation, Lennander-Vorlesung. *Svenska läk.-sällsk. handl.*, 62: 107–150, 1936.

SIMULTANEOUS RUPTURE OF A PRIMARY OVARIAN PREGNANCY AND AN OVARIAN CYST

HEMORRHAGE FROM EACH OVARY—REPORT OF CASE

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OVARIAN pregnancy, while rare, does occur and has been reported occasionally in the literature. "Primary ovarian pregnancy," according to R. M. Mayne, is termed, "that type of gestation which takes place in the structure of the ovary, the fertilization of the ovum before its liberation from the Graafian follicle, with subsequent development of the embryo entirely within the substance of the ovary. . . . ovarian pregnancy may take one of several courses. Full term pregnancy with the living fetus after operation has been reported in the literature. The most usual course is an early ovarian abortion. This is followed by slight or severe intraperitoneal hemorrhage. The embryo is rarely found in these ovarian abortions, but chorionic villi are."

The case herewith mentioned is most rare and very interesting due to the fact that in the same patient we encountered the rupture of an ovarian pregnancy on one side and an ovarian cyst on the other side with bleeding from each ovary.

CASE REPORT

Mrs. G. C., white, female, aged 27 years, weighing 180 pounds, had had no previous illness nor operation. She was married and had two children, 7 and 2 years of age, and denied abortions.

Her menses had started at the age of 11 years, were regular in occurrence and of the twenty-eight day type. Her periods were six or seven days in duration and without pain. The last menstrual period had occurred on time (May 12, 1937), two weeks before her admission to the hospital, and had been of normal length.

On May 26, 1937, at about 1:00 A.M., immediately following coitus the patient experienced a sharp pain in her abdomen, which caused her to become faint. The pain continued on and off throughout the entire morning and all that day. I saw the patient in consultation at about 6:00 P.M. eighteen hours after the first attack of pain. She had already been seen by her family physician who had diagnosed the case as appendicitis. The patient said that she had vomited and had taken two enemas with no let up of the abdominal pain. Excruciating pain was also present in area of right shoulder blade.

The abdomen revealed marked tenderness and rigidity; the rigidity was most marked on the right side and peritoneal rebound was present. A blood count in the afternoon showed 3,500,000 red cells, with a hemoglobin of 70 per cent. There were 16,400 white cells of which 80 per cent were polymorphonuclears, and 10 bands were present. Immediate hospitalization was ordered.

Examination at the hospital revealed the following abnormal findings: the heart and pulse rate were 120 per minute. Tenderness and rigidity were marked throughout the entire abdomen, and there was also marked peritoneal rebound. All these findings were more pronounced in the right lower quadrant. The urinary findings were negative. Bulging and tenderness were present in both vaginal fornices and also rectally. The blood count at this time showed 2,900,000 red cells, with a hemoglobin of 60 per cent. White cells numbered 16,400, with 87 per cent polymorphonuclears.

Ruptured Graafian follicle with intra-abdominal hemorrhage was the writer's diagnosis preoperatively.

At operation, a subumbilical midline incision was made to and through the peritoneum. The abdomen was found full of free blood and blood clots. The right ovary was enlarged to the size of a walnut with a bleeding hemorrhagic area in the center. The left ovary was also enlarged and bleeding, but its size could not be determined because it was edematous and

entirely open, with the appearance of a blow-out in a rubber balloon. The uterus was slightly enlarged, freely movable, located in an anterior position, not ruptured or punctured. Both tubes appeared normal. The appendix and other viscera were not examined. Free blood in the amount of 750 c.c. was syphoned from the abdomen, and an unknown quantity was soaked up in lap pads.

Due to the age of the patient (27 years) I hemisected each ovary, removing the hemorrhagic mass in the right ovary and the edematous cystic part of the left ovary, controlled the bleeding in each, and closed the abdomen in layers, without drainage. The specimens were sent to the laboratory. 600 c.c. of whole blood were given by direct method. The operation was performed under gas-oxygen-ether anesthesia in forty-five minutes, with the patient in Trendelenberg position throughout the operation and for the next forty-eight hours. The pulse rate at the close of the operation was 120 per minute, with the blood pressure at 115/50.

Postoperative Care. Nothing was given by mouth for the first twenty-four hours. Morphine sulphate was administered every four hours. Catheterization was performed every ten hours. Saline solution, 3,000 c.c., every twenty-four hours was given. On the second day after operation, the hemoglobin was 52 per cent and the red cells 2,560,000 in number. Other measures included iron and ammonium citrate, whiskey, and a light diet after the fourth day. The temperature ran up to 102, with the pulse at 120 per minute during the first forty-eight hours, but from the fifth day until the time of discharge, the temperature and pulse rate remained normal.

All the sutures were removed on the ninth day. The wound remained clean throughout, and the patient was out of bed on the tenth day. At no time was the abdomen distended. The blood pressure at all times remained about 115/50, and on the ninth day stayed at 100/50. The patient was discharged from the hospital on June 8, 1937, having completely recovered except for a secondary anemia.

The pathologic diagnosis was: ruptured right ovarian follicular cyst with pregnancy; ruptured left ovarian cyst; intra-abdominal hemorrhage.

Pathologic Report. Dr. William Hala, Pathologist at the hospital, presented the following report:

"*Gross description:* Specimen consists of both ovaries, one collapsed, other showing a ruptured hemorrhagic cyst.

"*Histologic:* Section of smaller ovarian cyst, which was collapsed when received, shows a single follicular type of cystoma. Examination of larger ovarian cyst grossly shows a ruptured hemorrhagic area disclosing the presence of an ectopic gestation, without doubt primary in the ovary. There is first a lining of trophoblasts in the cyst wall. The contents of the cyst consist of coagulated blood and numerous well developed chorionic villi. Elsewhere this ovary shows the presence of single follicular cysts."

REFERENCES

Mayne, R. M. Ovarian pregnancy. Report of a case. *J. Iowa State Med. Soc.*, 16: 282–284, 1926.

Like, L. E. Ovarian pregnancy. *Am. J. Obst. & Gynec.*, pp. 643–645.

SUPPURATIVE PERICARDITIS

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Introduction. Suppurative pericarditis is much more common than is ordinarily thought. Most cases, however, are found as a complication to pneumonia, and are usually discovered at autopsy. Since cases clinically diagnosed and successfully treated are comparatively rare even yet, I presume to report this case. Another reason is to outline and emphasize certain factors, and particularly to recommend a surgical approach which, although it is not new, has not generally been adopted.

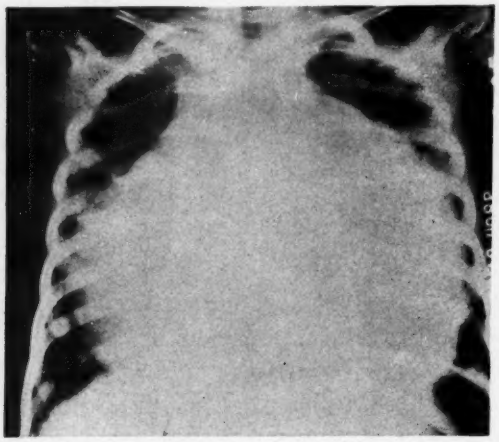

FIG. 1. Shows the tremendous enlargement of the heart shadow. Note the unusual persistence of the pericardio-phrenic angle on the right side.

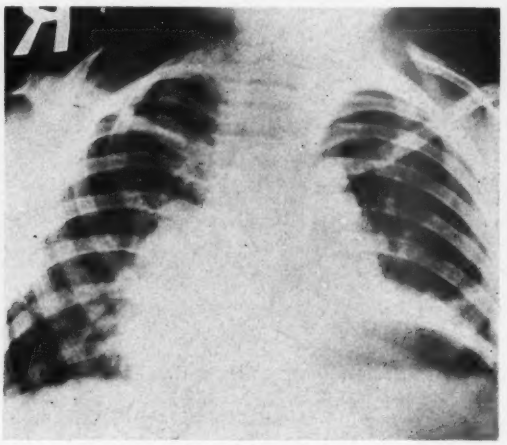

FIG. 2. The cardiac shadow is much reduced in comparison with Figure 1.

Treatment of purulent pericarditis is necessarily surgical. It is permissible to aspirate for diagnostic purposes and possibly for palliative treatment.

Technique of Aspiration. It may be noted that when the pericardium fills with pus the heart "floats" forward; therefore a needle, when introduced, may easily enter the heart muscle or may damage one of the coronary vessels. Aspiration is sometimes done to the right of the sternum and in this area the needle might even tear the thin auricular wall of the right auricle. When aspiration is necessary, it is the writer's belief that the fifth interspace in the midclavicular line is the safest. The needle is directed upwards and slightly outwards to keep the point from approaching the heart itself. It is quite obvious that this method could not possibly drain adequately the posterior part of the pericardium, known as the oblique sinus.

Difficulties of Draining the Pericardium. Drainage of the pericardium usually is accomplished by resecting a portion of the costal cartilages of the fourth or fifth ribs near the sternum, opening the pericardium and inserting a rubber tube or Penrose drain. This obviously gives inefficient drainage, since adhesions form readily and, as pointed out above, the heart rides forward against the anterior pericardial wall. It is rather a far cry to the large dependent sac behind the heart called the oblique sinus, which is difficult or impossible to drain in this way. A more rational method of drainage is reported in the following:

CASE REPORT

The patient, a young boy aged 5 years, (#2530) had been healthy with the exception of whooping cough fourteen months previous.

350 c.c., was removed by aspiration. This pus had the consistency and approximately the color of milk or very thin cream. Cultures were taken. The child immediately was relieved.

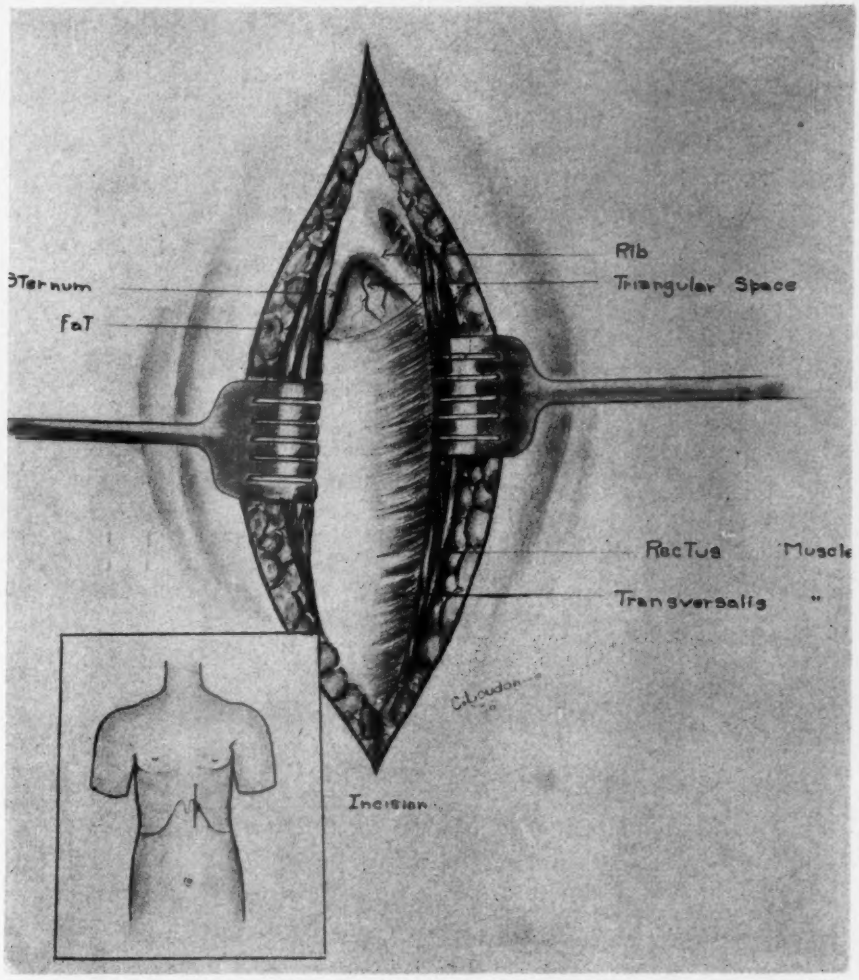

Fig. 3. The small figure shows the incision. The larger figure shows the incision retracted to disclose the anatomy involved. The ends of the costal cartilages may be removed if additional space is required.

The present illness had begun twelve days before with sore throat and a generalized malaise, resembling influenza. The child became very short of breath and somewhat cyanosed and had to be propped up to get his breath. The attending physician stated that for four days he had heard a rub which he thought was pericardial.

The patient was sent to the Queen of Angels Hospital. An *x*-ray picture showed a shadow which was obviously the heart, but because the pericardiophrenic angle was not obliterated, it was thought at first that it might be a very large heart. (Fig. 1.) However, the needle was inserted in the fifth space, midclavicular line on the left side, and a large quantity of pus, about

Aspiration was repeated on the following day, getting the same large quantity of fluid. On the third day the boy was operated on.

Operation. Local infiltration of 1 per cent novocaine was the only anesthesia used.

The incision was about 4 inches long through the costosternal angle, continuing up over the ribs about 1 inch and vertically downwards over the rectus muscle. The incision was carried through the anterior sheath of the rectus, and the rectus muscle was split and retracted. This exposed the posterior sheath of the rectus, made up of the transversalis, which is muscular in this particular place. (Fig. 3.) Continuing in the angle between the xiphoid process of the sternum and the costal cartilages, the finger

comes into a triangular space bounded by the sternal attachment of the diaphragm, the posterior sheath of the rectus and the costal attachment of the diaphragm. (Figs. 4 and 5.) Continuing up in this area, the finger passes over a rounded edge which represents the upper border of the diaphragm where it becomes continuous with the posterior sheath of the rectus. The finger may feel the pericardium, and if directed backwards and downwards, may feel the upper free border of the diaphragm. It may be noted that upwards through this area is continuous with the anterior mediastinum which is not definitely walled off, the pleura

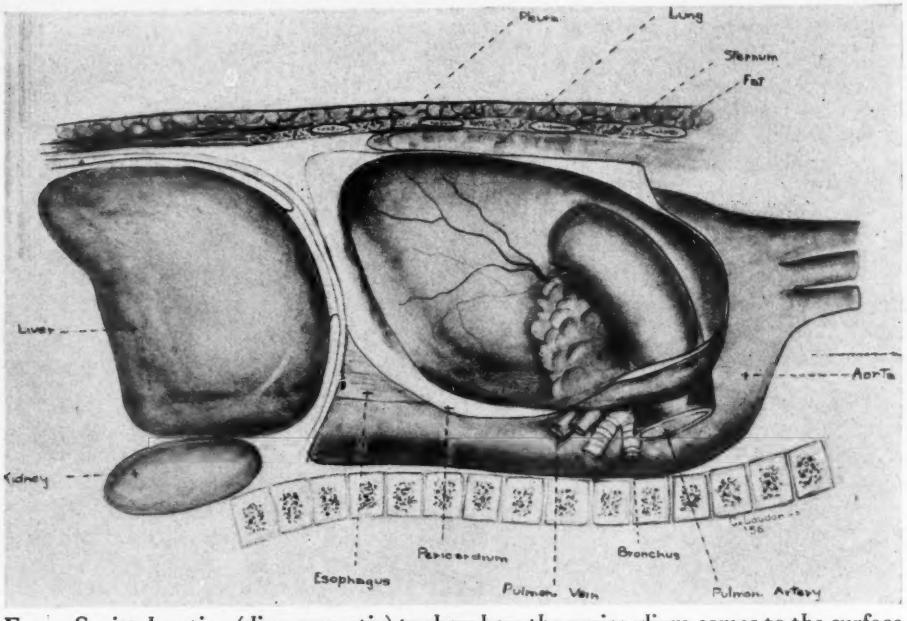

FIG. 4. Sagittal section (diagrammatic) to show how the pericardium comes to the surface in the triangular space.

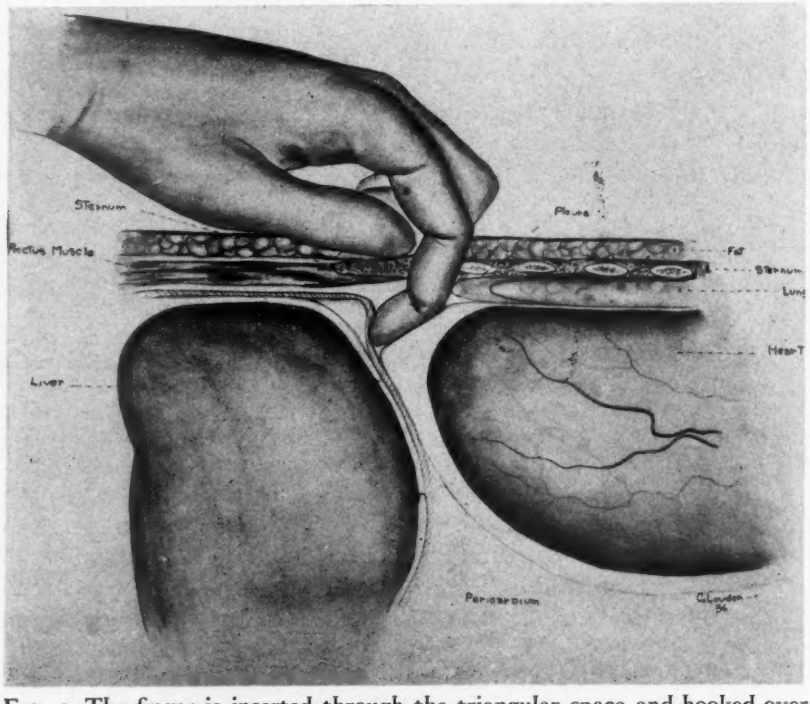

FIG. 5. The finger is inserted through the triangular space and hooked over the upper free border of the diaphragm, pressing on the pericardium.

and lungs coming down on either side. The writer, therefore, did not open the pericardium at this stage but packed the area with gauze to promote adhesions in the anterior mediastinum. The gauze kept the wound open in the rectus, the lower part of which was sutured.

On the following day it was a simple procedure to remove the gauze and then open the pericardium. The finger was inserted to break down adhesions in the pericardial cavity, but in this case there did not appear to be any. A soft tube was guided into the pericardium and down posteriorly to the heart into the oblique sinus, with a stitch in the fascia to hold the tube in position. A large quantity of pus was evacuated.

The patient left the table in good condition. He was much improved; a second *x*-ray showed the pericardium to be smaller. (Fig. 2.) The tube was removed forty-eight hours after the operation, early removal being prompted by the fact that the tube was rubbed by the heart at each beat. The pericardium continued to drain well, the action of the heart apparently forcing the fluid out. On the second day the patient was placed on his face to allow the best possible postural drainage—this is considered to be a very important feature. Drainage gradually became less and ceased on the tenth postoperative day. Apparently no recurrence of fluid in the pericardium occurred and subsequent *x*-rays showed on enlargement of the heart. The patient did develop some dulness in the base of the left lung and some pleuritic effusion was present, but this absorbed without aspiration. Pulse and temperature came down to normal. The child returned home on the thirty-fifth day.

Follow-Up. The boy has done exceedingly well and is reported in excellent health two years later.

Bacteriology. The report of Dr. Roy W. Hammack is as follows: "Fluid examined is pericardial. General characteristics: large amount of thick green pus.

"Method of examination. Gram stain of the smear showed numerous pus cells and a few small Gram-negative bacilli. Cultures, June 20 and June 22, 1935, were made on Rosenow's blood and blood-agar plates. A growth of nonmotile Gram-negative short, oval bacillus developed in the brain broth culture in twenty-four hours. No growth occurred on the blood agar plates.

"After transplanting several times in brain blood to which a small amount of sterile blood was added, a more luxuriant growth developed.

"Conclusion: no change in carbohydrate media. This organism has the appearance of B. pertussis."

SUMMARY

1. A case of purulent pericarditis successfully treated by operation is reported.

2. Emphasis is placed on the value of draining these patients by splitting the rectus muscle and approaching the pericardium from below, thus giving dependent drainage to the oblique sinus.

3. It is dangerous to try to treat these cases by repeated aspiration.

4. Early removal of the Penrose drain or tube from the pericardium is urged.

5. Emphasis is placed on the importance of postural drainage. It has been stated that these cases will drain well by postural drainage alone.

6. The author has described the anatomic relations which enter into this discussion.

PARASAGITTAL MENINGIOMAS*

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IT is well known that the intracranial tumors which arise from the meninges are well circumscribed and can be completely removed. But it is also true that such a removal is not always accomplished easily. Because of their slow growth, meningiomas often attain considerable size without symptoms, they are frequently quite vascular, and in many instances they invade the dura mater and skull. With the possibility of a permanent cure of the disease in view, the surgeon has continued to work to overcome these obstacles and frequently is rewarded by a most satisfactory and lasting postoperative result. However, the tumors lying along the falx cerebri on either side of the mid-line—the so-called parasagittal meningiomas—through their very location present particularly difficult problems in diagnosis and in treatment. It is these problems which we wish to discuss briefly here.

CASE REPORTS

CASE I. M. C., white female, aged 59, reported a mass on the top of the head, progressively enlarging over a period of nine years, accompanied by convulsive seizures during the past seven months.

Present Illness. Nine years before admission the patient noticed a small lump on the top of her head. Her physician advised her that it was probably a cyst of the scalp which she should have removed if it enlarged. When she next consulted him the mass had enlarged to the size of a lemon and was obviously not an ordinary sebaceous cyst. During the seven months prior to admission the patient had had four or five attacks of Jacksonian epilepsy involving the right foot and leg.

Examination. The patient was a rather obese woman with mild cardiac enlargement, a blood pressure of 170/80, and a mass measuring 6 × 3 × 1½ inches near the vertex of her skull. She showed scattered neurologic signs, including a slight weakness of the right extremities, a slight left-sided ptosis, and a small left homonymous defect in her visual fields. The *x*-ray (Fig. 1) disclosed extensive changes in the vault of the skull, thought to be due to invasion by a meningioma or a cholesteatoma.

Operations. Biopsy showed the tumor to be a meningeal fibroblastoma. At the first stage operation the involved bone and a portion of the underlying tumor were removed by Dr. C. H. Frazier. (Fig. 2.) At the second stage (five months later) a meningeal fibroblastoma lying along the left side of the falx cerebri in the parietal region was extirpated by the author.

The patient had considerable right-sided weakness for a few weeks after operation. Several months later she had a few brief twitchings of the right foot, but was free of symptoms five months postoperatively.

Comment. The enormous extent of the bone involvement in this patient forced the removal of a large bone flap which left a correspondingly large skull defect. The suspected area was thoroughly coagulated with the electrosurgical unit, but it is impossible to say whether all cells were destroyed. In a woman of 60 it is doubtful whether the skull defect or a possible very slow recurrence would represent any real hazard, but obviously, either might be serious in a younger individual.

CASE II. M. P., white, female, 58, had a left occipital parasagittal meningioma which was removed in 1918, in 1930, and again in 1936. The bone was not involved, but invasion of the falx led to an incomplete extirpation on each occasion.

* From the Neurosurgical Service, Landon Surgical Clinic, Western Pennsylvania Hospital, Pittsburgh, Pennsylvania. Read at a meeting of the Allegheny County Medical Society, Pittsburgh, Pennsylvania, November 16, 1937.

History. On her first admission in 1918 (at the age of 40) the patient's failing vision, headaches, staggering, and right homonymous hemianopsia led to the diagnosis of a left occipital brain tumor. A left parasagittal meningioma 4 cm. in front of the pole of the occipital lobe was found and removed by Dr. C. H. Frazier. Symptoms of a recurrence began to appear ten years later and in 1930 a tumor measuring 7 × 6.5 × 5.5 cm. was removed by Dr. Frazier. He noted the infiltration of the falx and feared a recurrence. The patient developed weakness of the right extremities, attacks of dizziness, impairment of memory and vision in 1935 (at the age of 58) and was operated upon for the third time in 1936 by the author.

Operation. A very large tumor principally on the left side of the falx but straddling its lower edge to extend across the midline was found, and a considerable portion extirpated.

Course. The patient's convalescence was uneventful after a rather stormy first twenty-four hours. Eight months later she was greatly improved mentally and in the strength of her right side, but was still slightly forgetful and had begun to drag her left leg slightly.

Comment. In this case the absence of bone involvement enabled the operators to replace the bone flap three times without risk, but the invasion of the dura led to recurrences in ten and five years respectively. Furthermore, the last recurrence was so extensive as to preclude the possibility of radical removal of the tumor.

Fig. 1.

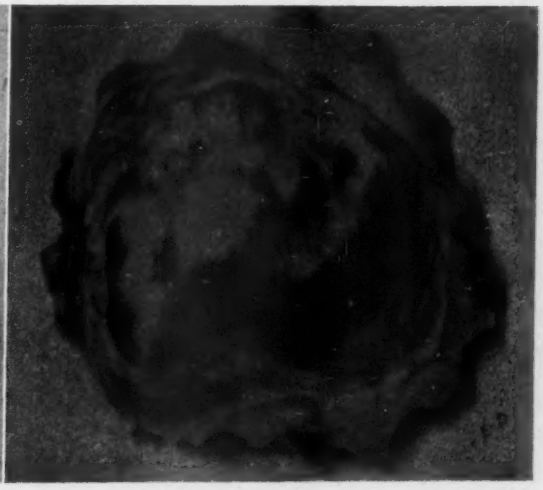

Fig. 2.

Case III. W. R., white, male, 27 (referred by Dr. William Anderson), had had a slowly enlarging "bump" near the vertex of the skull for about one year. No neurologic findings were noted except early papilledema. At operation a bilateral frontoparietal parasagittal meningioma was removed with the portion of the falx and superior longitudinal sinus which it invaded. The involved bone was boiled and replaced.

History. For one year the patient had been aware of a slowly enlarging firm swelling near the vertex of his skull. (Fig. 3.) One month before admission he began to notice a momentary clouding of his vision when he changed his position quickly, as in getting up from a chair.

Examination. Neurologic examination was entirely negative with the exception of a swelling (apparently bony) about 2 × 3 inches along the midline of the head in the parietal regions, and bilateral papilledema. *X*-ray disclosed a thickening of an area in the parietal portion of the skull, showing a definite vertical striation.

Operation. A scalp flap was reflected around the bony swelling with the base to the right and posteriorly. The involved bone was surrounded by burr holes and excised. (Fig. 4.) Upon opening the dura it became apparent that the underlying tumor lay along both sides of the falx and involved this structure, the superior longitudinal sinus, and the overlying dura. After some consideration the sinus was ligated and cut anterior and posterior to the lesion and the tumor with all of the involved dura removed. (Fig. 5.) The bone flap was

boiled for ten minutes and replaced, being wired in place. The scalp was closed as usual.

Course. The patient made an uneventful recovery and was able to resume his duties as

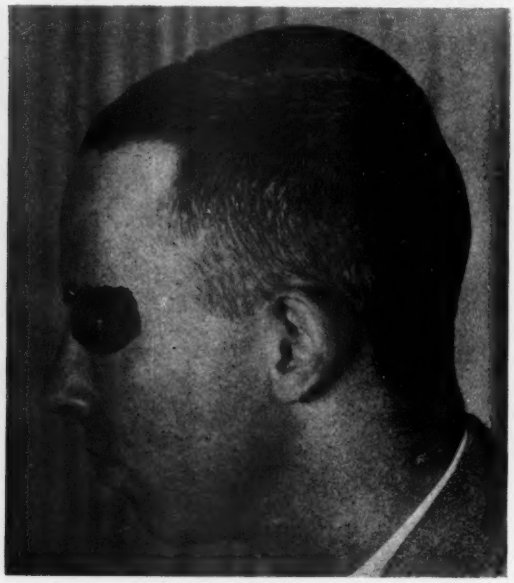

FIG. 3.

a teacher when school opened two months after his operation.

DISCUSSION

The symptomatology of parasagittal meningiomas naturally varies with the position of the lesion along the falx and in general coincides with the symptom complex of the lobe involved—frontal, parietal, or occipital.

Two characteristics, however, seem worthy of emphasis. The first is the very early bone invasion when the tumor is near the surface; or, stated in another fashion, the frequent association of very extensive involvement of the skull with a relatively small intracranial tumor. In both Case I and Case III of this report, the operator was surprised at the comparatively small size of the tumors found beneath the very large bony swellings. A second characteristic which is perhaps in a large measure dependent upon the first, is the late appearance of neurologic symptoms or signs in case of meningiomas along the falx. In Case III, for example, no neurologic changes whatsoever could be detected though the bony swelling had been present for one year and in spite of the fact that the tumor found at operation pressed upon the sensory and motor cortical areas bilaterally.

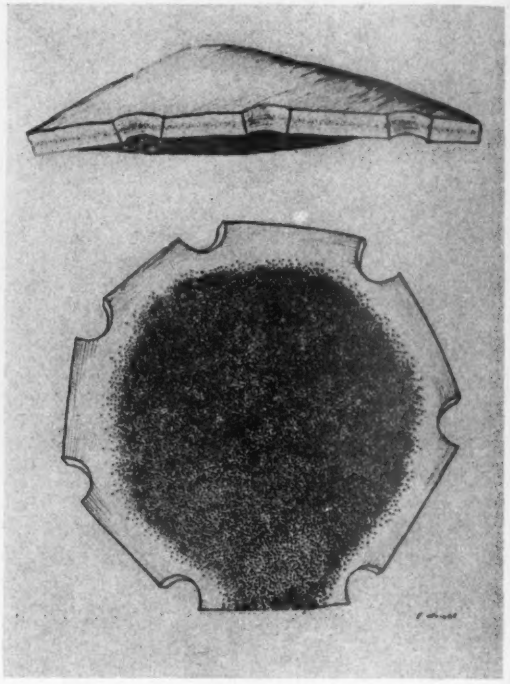

FIG. 4.

The remaining features of the symptomatology are essentially those of meningeal fibroblastomas in any location, namely: slow growth, often a history of convulsive attacks, and the late development of symptoms or signs of increased intracranial pressure. These need not be dwelt upon here.

The resection of a portion of the superior longitudinal sinus is a procedure which may be regarded as at least somewhat hazardous. Nevertheless, a number of reports in the literature[1,2,3] attest the fact that it can be carried out without producing any detectable change in the patient. As in the ligation of any large vessel, the sequelae of tying the longitudinal sinus seem to depend largely upon the adequacy of the collateral circulation. This in turn depends upon (1) the point at which resection is carried out, and (2) the existence of previous thrombosis from tumor invasion. It is generally agreed that such thrombosis is usually present in cases of

meningioma (although unfortunately there are no available histologic studies to prove it) and that in such cases any part of the sinus can be resected with impunity. If no such thrombosis exists, ligation of the anterior third can be done without fatality, but in some cases this has been followed by transient mental changes.

Boiling of portions of the skull to kill invading neoplastic cells or organisms was described by Naffziger[4] in 1936. He reported the successful use of the procedure in several cases of meningioma and osteomyelitis. In Case III this method was employed to avoid creating a large skull defect in a young male patient—a defect, moreover, which would have exposed a considerable part of both motor areas to possible injury.

SUMMARY

1. Three cases of successfully operated parasaggital meningioma are described. Their characteristics, (1) early involvement of overlying bone, and (2) the late development or total absence of neurologic symptoms, are stressed.

2. In one instance the very extensive bone involvement necessitated the creation of a large skull defect.

3. In a second the third recurrence of the tumor was found to be so large that only a partial removal could be effected.

4. In a recent case a complete extirpation of a bilateral parasaggital meningioma was carried out successfully by resection of all of the involved dura—including several inches of the superior longitudinal sinus, and a portion of the falx. The widely invaded overlying bone was resected, boiled, and replaced. This technique seems to offer a permanent cure without producing a postoperative skull defect.

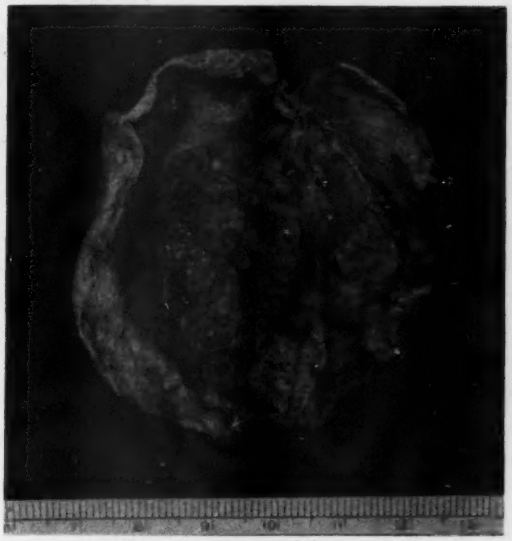

Fig. 5.

REFERENCES

1. Towne, E. B. Invasion of the intracranial venous sinuses by meningioma (dural endothelioma). *Ann. Surg.*, 83: 321–327 (March) 1926.
2. David, M., and Bissery, Brun M. Sur un cas de méningiome de la faux opéré avec succès. Absence de troubles paralytiques apres résection du sinus longitudinal au niveau de l'abouchement des veines rolandiques. *Rev. neurol.*, 1: 725–730 (May) 1934.
3. Tönnis, W. Die Zulässigkeit der Resektion des Längsbluteiters des Gehirns. *Deutsche Ztschr. f. Nervenh.*, 136: 186–189 (March) 1935.
4. Naffziger, H. C. The restoration of defects in the skull. *Ann. Surg.*, 104: 321–331 (Sept.) 1936.

CARCINOMA OF THE BREAST AND PREGNANCY

A REPORT OF THREE CASES

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THREE cases of carcinoma of the breast associated with pregnancy have occurred on the obstetrical service of the Long Island College Hospital during the past two years. One would ordinarily expect some effect of pregnancy on a neoplasm of the mammary gland, an organ which normally undergoes marked hyperplasia during pregnancy. A survey of the literature, however, shows a marked difference of opinion as to the effects of pregnancy on cancer of the breast. Presentation of these three cases may aid in formulating a more definite opinion.

CASE I. Miss S. I., a 34 year old white spinster, was admitted on May 8, 1930. She had first noticed a small lump in the right breast one year prior to admission. The tumor was excised by her physician during August 1929 and a course of *x*-ray therapy given.

Examination on admission showed a recurrent tumor mass beneath the old scar. A radical mastectomy was then performed. Pathologic examination revealed chronic interstitial mastitis and a duct cell carcinoma. The wound healed by primary union and she was discharged on the eighteenth day following operation.

The patient was readmitted on January 13, 1935, because of a recurrence in the other breast. This was first noted as a small, hard mass the size of which remained stationary for nearly two years and then increased. Examination showed a firm, immobile, nodular, oval mass in the left breast. An amputation of the left breast was performed after a preliminary course of twenty-six *x*-ray treatments were given. The pathologic diagnosis was alveolar carcinoma of duct origin. She was discharged on May 26, 1935, with the left breast wound healing by primary union.

The patient was again readmitted on December 10, 1935, when she stated that she had felt well and strong since her last admission and had gained in weight. The last menstrual period was during September 1935. At the beginning of December, the patient suffered vaginal bleeding and lower abdominal cramps which continued intermittently until the time of admission. A preoperative diagnosis of incomplete abortion was made and a curettage performed. The pathologic diagnosis was decidual endometritis and incomplete abortion. It was estimated that the patient was about three months pregnant.

During the two week period after her return home the patient's general condition rapidly became worse. She suffered from continued weakness and soon became bed-ridden. Examination revealed marked swelling of the abdomen, generalized jaundice, dehydration and dyspnea. She was readmitted at this time and died two days later. Post-mortem examination showed generalized carcinomatosis.

In the opinion of the attending physician who saw her from the onset and in all stages of her illness, the growth and spread of the tumor were markedly increased by the occurrence of the pregnancy.

CASE II. Mrs. M. N., 42 years of age, gravida V, para IV, was admitted on June 29, 1937, for recurrent carcinoma of the breast and pregnancy. Six years previously the patient had noticed a small lump in her right breast. Two years later she gave birth to her fourth child and failed to observe any change in the tumor during pregnancy or lactation. In 1934, the tumor became larger and a radical mastectomy was done. This was followed by six *x*-ray treatments and the application of radium. Her condition was surprisingly good up to the third month of the present pregnancy, at which time she came under our observation. Within the next few months, the patient grew rapidly worse, suffered from a persistent cough and lost 33 pounds.

On admission, she was emaciated and cyanotic. The veins of the neck and face were distended and three recurrent carcinomatous

ulcers were observed at the site of the old mastectomy scar. *X*-ray examination revealed a moderate amount of fluid in the pleural cavities. The uterus was the size of a six months' pregnancy and the fetal heart was heard distinctly. *X*-ray therapy according to the Coutard technique was given. The patient is still pregnant and expects to be confined within a short time.*

The attending physician, who has followed this patient from the onset of her illness, states that a marked change for the worse was noted in the patient soon after the beginning of her present pregnancy. This is contrary to the observation made in the course of her pregnancy four years previously, at which time little change in the tumor was noted. This case, however, may represent an instance of carcinomatous change in a fibroadenoma.

Case III. Mrs. F. C., a 35 year old Puerto Rican, para III, was admitted to the prenatal clinic on August 30, 1935. She was about six months pregnant. Physical examination of the breast was negative save for the usual signs of pregnancy. She was admitted to the hospital on January 7, 1936, and delivered spontaneously a normal full term infant. At this time, two large tumor masses were palpated in the left breast. Two weeks later, one of these was excised. Histologic examination revealed the tumor to be an extremely malignant and rapidly growing medullary carcinoma. The patient refused permission for a radical mastectomy and left the hospital against advice.

She was readmitted on October 22, 1936. During the interim of nine months, she had lost considerable weight, had aged considerably, and became too weak to perform her ordinary household duties. The tumor mass left in the breast had become very extensive. On October 28, 1936, a radical mastectomy was performed. The pathologic examination revealed essentially the same type of tumor as noted previously. She was discharged from the hospital on November 18, 1936, and is at the present time receiving a course of *x*-ray therapy. Examination recently showed improvement in her general condition and a recurrence of the tumor at the site of the operation.

This case is an instance of rapidly growing cancer of the breast associated with pregnancy. While it is conceivable that a small tumor may have been present at the time the patient first visited the prenatal clinic, it is hardly likely that a tumor of any large size would be missed. However, on admission to the hospital four months later, examination showed two large tumors. Her refusal to permit a radical mastectomy after one of the tumors was excised for diagnosis gave us a good opportunity to observe its rapid growth. The recent general improvement of the patient may be ascribed not only to the treatment but possibly to the fact that there is no longer the influence of pregnancy or lactation.

* This patient has since carried to term and delivered an infant spontaneously. She died within one week post-partum. The child is alive.

It was formerly universally agreed that pregnancy has a stimulating effect on all tumor growth and especially on the growth of mammary carcinoma. Reference to the literature demonstrates many case reports where it appears unquestioned that pregnancy and lactation stimulated the growth of the neoplasm and were responsible for early fatalities. In some instances, the patient survived only a few months after a small tumor was palpated.[1,2,3] These authors believed that the abundant vascular and lymphatic circulation of the breast during pregnancy and lactation offered peculiarly widespread channels for extension. While it is also suggestive that direct hormonal stimulation of the growth of the cancer occurs in the same manner in which normal mammary gland cells proliferate during the premenstrual phase of the sexual cycle and during pregnancy, there is no direct evidence for this belief. According to Loeb,[4] mammary gland cells that have undergone definite carcinomatous transformation are no longer responsive to normal hormonal stimulation.

On the other hand, one of the larger series of cases presents a number of five years survivals that corresponds very closely with that of the nonpregnant group.[5] It must also be remembered that in the age group in which pregnancy usually occurs, namely the young, cancer of the breast has generally been regarded as having a notoriously bad prognosis.

A consideration of the three cases reported here confirms the generally accepted belief that pregnancy stimulates the growth of cancer of the breast and hastens a fatal outcome. A safe view would be to regard pregnancy and lactation as probable aggravating factors in all cases of cancer of the breast which especially call for early diagnosis and treatment.

SUMMARY AND CONCLUSIONS

1. Three cases of cancer of the breast associated with pregnancy have occurred on the obstetrical service of the Long Island College Hospital during the past two years.

2. Survey of the literature shows a divergence from the universally held belief that pregnancy markedly stimulates the growth of mammary carcinoma.

3. Clinical analysis of the three cases herein reported shows a definite stimulating effect of pregnancy on cancer of the breast.

4. The differential diagnosis of a lump in the breast during pregnancy and lactation is of the greatest importance. Any reasonable doubt calls for biopsy and microscopic diagnosis.

I am deeply indebted to Drs. Vincent P. Mazzola and Grover C. Emery for their kind permission to publish two of the cases reported here.

REFERENCES

1. Wachsmuth, W. *Chirurg*, 5: 585, 1933.
2. Rubinacci, G. *Rossegna internaz. di clin. e. terap.*, 11: 753, 1930.
3. Lee, B. J. *Am. J. Obst. & Gynec.*, 20: 775, 1930.
4. Loeb, L. In Cowdry, E. V. Special Cytology, 3: 1667. New York, 1932. Paul B. Hoeber.
5. Kilgore, A. R., and Bloodgood, J. C. *Trans. Sect. Surg. Gen. & Abdom., A.M.A.*, p. 333, 1928.

PARAGEUSIA AS A SYMPTOM OF KIDNEY DISEASE*

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OF the many symptoms which a patient may present, perhaps none is more baffling than that of disturbance of taste. It has been noted as an accompanying symptom of a number of disease syndromes.

Wildner[1] noted a frequent association of taste disturbance in gastrointestinal and biliary disorders, and in diabetes, and he reported its occurrence in a case of pancreatic abscess. Stout[2] reported an association of parageusia with calculus of the submaxillary gland. Barnes[3] reported parageusia in a patient with a chronic otitis media, which was relieved after a mastoid operation. Brain tumors and diseases of the nervous system have been noted as causes of parageusia, and in local diseases within the mouth, pyorrhea, heavy metal poisoning, and the like, disturbance of taste is not uncommon.

A number of texts on diagnosis and urology do not list disturbances of taste or parageusia in their indexes, and French,[4] while he gives a good discussion of the symptom, makes no mention of it in association with urinary tract disease. Reilly,[5] however, reported a case in which parageusia occurred within an hour after the onset of kidney colic, and he noted parageusia so frequently in association with hypertension that he wrote, " . . . close questioning of all patients with high arterial tension and other evidences of nephritis has practically always revealed the presence of the symptom of persistent bad taste."

In most instances parageusia occurs in association with other symptoms, or some fairly evident pathology, but when it is the patient's sole complaint, the diagnosis is apt to be quite obscure, as the following protocol illustrates.

CASE REPORT

On December 26, 1934, after a year of migratory, rheumatic pains in shoulders, knees and chest, J. M., 58, male, teacher, had his chronically infected tonsils removed under local anesthesia. There was some post-operative bleeding the afternoon of the operation, but recovery was otherwise uneventful.

On March 14, 1935, the patient came to the office with a complaint of a peculiar taste, insidious in onset, and of about six weeks' duration, which he thought came from the back of his mouth, and from the left side more than the right. It was described as a sweetish-sour, metallic taste, resembling that of sheep-sorrel (Rumex Acetosella), a plant he had chewed during his boyhood on the farm. It had no relation to meals, nor to any particular foods. The patient felt that the taste was related in some way to the tonsillectomy as it had never been present prior to the operation.

Examination of the nose, ears, and mouth, including palpation of the salivary glands and probing of the left parotid duct, failed to account for the symptom. A careful history and physical examination revealed nothing of pathologic interest except a slight elevation of the blood pressure which was 154/90.

A variety of gargles and chewing gums was tried without improvement or notable relief. A dental consultant had nothing to suggest. After six months, on September 10, 1935, the patient reported that his unpleasant taste was still present, although he felt well otherwise.

On January 9, 1936, the patient was seen at his home. He complained of abdominal pain accompanied by marked distention, but there was no localized tenderness. Treatment was symptomatic and the patient promptly recovered. On March 9, the patient had a somewhat similar attack, in which there was an aching pain and some tenderness in the left lumbar area. A specimen of urine showed neither albumin nor sugar, while microscopic analysis disclosed 10 to 15 W.B.C. and a few epithelial cells.

* From the Department of Surgery, Washington University School of Medicine.

A week later a flat *x*-ray picture showed an opacity about 1 cm. in diameter in the left kidney area. The patient was quite comfortable and continued his teaching, with weekly check-ups of the urinary findings. On March 20, there were 30 to 40 R.B.C. per high power field, but this decreased to 10 to 15 R.B.C. per high power field by May 11, 1936.

Cystoscopy was done May 16, 1936. A 6 F. catheter was easily passed up the right ureter; the collected specimen was negative, and phenolsulphonephthalein excretion was 12 per cent. A 5 F. catheter stuck in the left ureter about 5 cm. above the ureteral orifice; a collected specimen showed an occasional cell, and phenolsulphonephthalein excretion was only 10 per cent. A right pyelogram was essentially normal, but on the left there was a shadow (stone) in the kidney pelvis, deformity of the upper calyx, suggesting a tumor, and hydroureter above the point of constriction. There was no reaction to the cystoscopy and the patient returned to work. Parageusia was present during this entire period.

On June 13, 1936, an operation was performed under spinal anesthesia. A thin-walled solitary cyst (congenital) about 4 inches in diameter and containing serous, straw-colored fluid was removed from the upper pole of the kidney. The stone was removed from the kidney pelvis and the wound closed with drainage.

The post-operative course in the hospital was quite smooth, but the urine was loaded with pus. This was decreasing in amount under urinary antiseptics and the patient had returned home, when he developed an acute right epididymitis with chills and fever. Under conservative treatment this condition gradually improved, and, at the same time, the bitter taste disappeared. On October 22, 1936, the patient was feeling well, his urine was free from pus, and he had gained 8 pounds. Subsequent specimens were examined at intervals and were negative.

The patient had a chill on May 19, 1937, following an upper respiratory infection of several days duration. He volunteered the statement that the bitter taste, which he had not noted for six months, had returned. A urine specimen was loaded with pus. On urinary antiseptics recovery was prompt. Cystoscopy was repeated June 19, 1937. The left pyelogram was essentially normal and a 9 F. catheter was passed up the left ureter without difficulty. Both ureteral specimens were essentially negative. Parageusia was no longer present.

Here, then, is a patient who developed parageusia about one year prior to the onset of symptoms which led to the investigation of the urinary tract. Correction of the pathology relieved the parageusia, but six months later, following an upper respiratory infection and the flare-up of a pyelitis, the parageusia returned, to disappear again, as the pyelitis itself subsided.

It seems evident that there was a relationship between the urinary tract pathology and the parageusia. The mechanism, however, is not clear. There could be, perhaps, a direct renal-gustatory reflex. Or, one can postulate the absorption of an unsavory substance from the kidney to the blood stream, which is conveyed to the taste buds directly, or by secretion into the saliva. A central stimulation of the taste buds does not seem so probable. It is not unlikely, however, that the real mechanism depends on the reflex gastrointestinal disturbance so frequently seen in urinary tract disease, and that stimulation of the taste sense is due to regurgitation of gastric content. Alvarez[6] has shown that regurgitation from the stomach to the back of the tongue is not uncommon, and such a mechanism would seem to explain the relationship in this case.

CONCLUSION

Disturbance of taste may be an early and single symptom of urinary tract disease, and in the absence of other evident cause, patients presenting a complaint of parageusia should have a painstaking examination of the urinary tract.

REFERENCES

1. Wildner, F. S. Notes on parageusia. *Am. J. Clin. Med.*, 31: 466, 1924.
2. Stout, P. S. Dry mouth, vile taste, calculus in submaxillary gland. *Laryngoscope*, 45: 962, 1935.
3. Barnes, L. Case of parageusia associated with chronic suppurative otitis media. *Ann. Otol., Rhin. & Laryng.*, 42: 909–910, 1933.
4. French, H. Index to Differential Diagnosis. Baltimore, Wm. Wood & Co., 1936.
5. Reilly, T. F. Parageusia and its treatment. *New York M. J.*, 100: 1061–1063, 1914.
6. Alvarez, W. C. The Mechanics of The Digestive Tract. New York, Paul B. Hoeber Co., 1928.

HYDRONEPHROSIS IN CHILDREN: REPORT OF TWO CASES*†

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INTRODUCTION

CONGENITAL ureteral obstruction is not uncommon in children. In a study of 2,420 pediatric cases coming to autopsy at Bellevue Hospital, Campbell[1] found ureteral blockage in approximately 2 per cent. Congenital ureteral obstruction may occur without urinary symptoms or findings, but persistent pyuria is the usual finding.

Early and proper relief of these obstructive conditions would prevent much renal damage and increase the life span of many children. The necessity of closer cooperation between the pediatrician and the urologist is obvious.

Two cases of hydronephrosis due to congenital ureteral obstruction are presented here, both of which are on the Pediatric Service of the New York Hospital and have been seen in consultation by the Department of Urology (James Buchanan Brady Foundation) of the Hospital.

REPORT OF CASES

J. C., a white male, was first seen in the New York Hospital on February 4, 1934, at the age of two months, at which time he was suffering from hematuria, dysuria, and urinary frequency of twelve hours' duration. The past history was unimportant.

Physical examination showed a well-developed, well-nourished infant who appeared acutely ill. The abdomen was distended and the left kidney large and easily palpated. The right could not be felt. The external genitalia were normal except for a phimosis.

Laboratory examination showed the urine to be cloudy and loaded with pus with specific gravity of 1.010, neutral reaction, and albumin 2+. The blood urea nitrogen was 38 mg. per 100 c.c., and the phenolsulphonephthalein output 5 per cent in one and one-half hours, with a total of 30 per cent in three hours.

FIG. 1. Retrograde pyelogram showing hypoplastic right kidney and dilated ureter.

Cystoscopy disclosed a pale bladder mucosa, the ureteral orifices in normal position, and constriction of the vesical neck. Pyelography revealed a hypoplastic right kidney with a somewhat dilated ureter and a markedly hydronephrotic left kidney with a tortuous hydro-ureter. Ten-minute phenolsulphone-

[1] CAMPBELL, M. F. Ureteral Obstruction in Infancy, *Am. J. Surg.* 5: 445, 1928.

* From the Department of Urology (James Buchanan Brady Foundation) of the New York Hospital.

† Presented before the Section of Genito-Urinary Surgery, New York Academy of Medicine, October 14, 1936.

phthalein excretion on the right side was 1 per cent and on the left 8 per cent. (Fig. 1.)

A left nephrostomy was recommended.

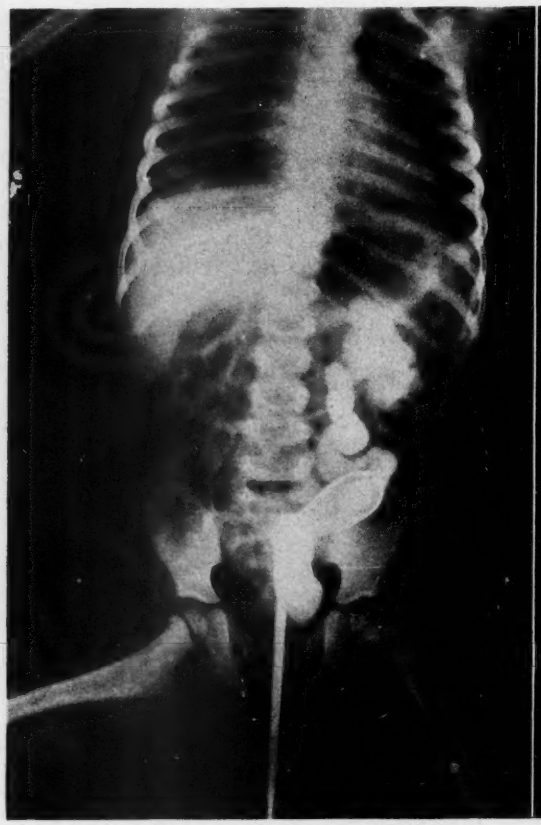

FIG. 2. Left hydronephrosis and hydroureter, with strictures at the ureteropelvic and ureterovesical junctions.

FIG. 3. Hypoplastic right kidney. Left hydronephrosis and hydroureter, with strictures at the ureteropelvic and ureterovesical junctions.

The patient improved under medical treatment, and was discharged eleven weeks after admission.

He was readmitted twenty-six months later because of a reaction following vaccination for smallpox. There had been no urinary symptoms in the interim, but urinalysis showed a trace of albumin, many granular and cellular casts, and many pus cells. The blood urea nitrogen was 25 mg. per 100 c.c. Cystoscopy revealed a normal bladder. Catheterization of the right ureter could not be accomplished, but the left ureter was readily catheterized. Bacilli coli were obtained by culture from the urine of the left kidney. Pyelography showed increased dilatation of the renal pelvis and ureter, with strictures at the uretero-pelvic and uretero-vesical junctions. (Fig. 2.)

The left ureter was drained for six days by means of a No. 5 French catheter. The child's condition improved and he was discharged to return for further treatment.

Six weeks later he was again admitted to the hospital. The dysuria and frequency had continued since his previous discharge, but the urine showed less pus than on the earlier admissions. The blood urea nitrogen was 17 mg. per 100 c.c.

Cystoscopy was again done; a No. 5 French ureteral catheter was placed in the left ureter for drainage and allowed to remain in position for five days. The child was then given a ketogenic diet for two weeks, during which time the *pH* of the urine remained about 5.6. Under this treatment his urinary symptoms improved, and he was discharged, to return in a month.

Five weeks later (Sept. 14, 1936) he was readmitted to the hospital because of intermittent attacks of chills and fever, associated with malaise, over a period of two weeks. Examination at this time showed the urine to be cloudy, with a specific gravity of 1.010, and

15 to 30 white blood cells per high power field. Pyelography revealed no changes in the right kidney, but the left pyelogram showed more

Fig. 4. Cystogram showing left hydronephrosis, dilated and tortuous ureter, and distorted ureteropelvic junction. Large indefinite mass in right kidney region.

marked dilatation of the kidney and ureter than upon previous examinations, with strictures at the uretero-pelvic and uretero-vesical junctions. (Fig. 3.)

A left nephrostomy, with correction of the ureteropelvic stricture, has been advised.

A. R., a white female, aged 6 years, was admitted to the New York Hospital on July 17, 1936, complaining of enlargement of the abdomen, abdominal pain, and headaches.

For several months the patient's mother had noticed that the child's abdomen was becoming larger, although she was losing weight. She had become fretful and listless, and at times complained of headaches and slight pain in the mid-abdomen. At no time had there been any urinary symptoms. The past history was irrelevant.

Physical examination showed a pale, thin child, apparently chronically ill. The abdomen was asymmetrically enlarged, with a mass occupying the entire upper right quadrant and extending into the right flank. There was no tenderness of the mass, but it was fluctuant and moved on respiration; it could be differentiated from the liver.

Laboratory findings were as follows: The urine

Fig. 5. Large hydronephrotic right kidney with destroyed cortex, and very narrow ureteropelvic junction.

was cloudy, with a specific gravity of 1.002; alkaline in reaction; showed albumin 2+; a few red blood cells and many white blood cells. The hemoglobin was 79 per cent; the red blood count 3,710,000; the white blood count 7,650; polymorphonuclear leucocytes 70 per cent; blood Wassermann negative. The blood urea nitrogen was 11 mg. per 100 c.c. and the blood sugar 92 mg. per 100 c.c. The total two-hour phenolsulphonephthalein excretion was 13 per cent.

Cystoscopy showed a normal urethra and moderate intrusion of the median portion of the vesical neck, with 20 c.c. of residual urine. The bladder mucosa appeared chronically inflamed; the ureteral orifices were in their normal position. The left ureter was catheterized, but the catheter failed to enter the renal pelvis. The right ureter could not be catheterized. Roentgenograms at this time showed a large left hydronephrosis, with a distorted ureteropelvic junction and a dilated and tortuous left

ureter. In the right kidney region was a large, indefinitely outlined mass. Intravenous urography revealed a functionless right kidney.

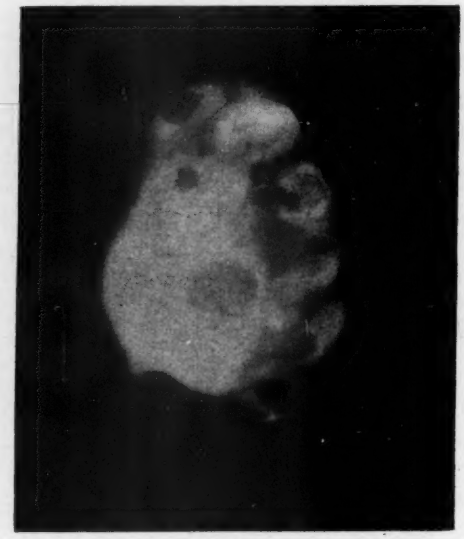

Fig. 6. Renal pelvis injected with opaque medium. Very thin cortex.

(Fig. 4.) Following the patient's admission to the hospital the right kidney rapidly increased in size, causing gastrointestinal and respiratory embarrassment.

Ten days after admission a right nephrectomy was done as an emergency measure, and a large hydronephrotic kidney, containing approximately 2,000 c.c. of clear straw-colored urine, was removed. The cortex was greatly thinned out, and there was a marked stricture at the uretero-pelvic junction, causing complete obstruction. (Figs. 5, 6, 7, and 8.)

Convalescence was uneventful, with persistent pyuria as the only urinary symptom. Cystoscopy was again performed and the left ureter catheterized without difficulty, but, as in previous attempts, the catheter failed to enter the pelvis of the kidney. A retrograde pyelogram showed poor filling of the kidney pelvis due to some uretero-pelvic obstruction. However, both the pelvis and ureter were considerably dilated. A culture of the urine from the left ureter showed *Bacillus subtilis*. The bladder was irrigated and the urethra dilated to No. 26 French. Further attempts to pass a catheter past the uretero-pelvic junction were unsuccessful. The blood urea nitrogen remained normal, but the urine continued to show a moderate amount of pus. (Fig. 9.)

Since the hydronephrosis was increasing, a left nephrostomy was done for drainage five weeks after removal of the right kidney. Investigation of the ureter showed it to be plastered onto the renal pelvis, forming an S-shaped kink with a narrow uretero-pelvic junction. The ureter was freed of adhesions and dilated with a No. 12 French ureteral catheter

Fig. 7. Photomicrograph × 130. Cross section of ureter at strictured area, showing thin wall and decrease in mucosa and muscularis.

Fig. 8. Photomicrograph × 130. Cross section of ureter below strictured portion, showing a more normal wall.

Fig. 9. Marked left hydronephrosis and dilated ureter, with a stricture at the ureteropelvic junction.

Fig. 10. Pelvis of left kidney injected with opaque medium.

through an opening made in the renal pelvis. A nephrostomy tube was inserted from within the pelvis through the cortex at the lower pole, and a No. 12 French ureteral catheter was passed through the nephrostomy tube and down the ureter for a distance of 10 cm. The pelvis was closed tightly and the kidney replaced in its normal high position.

Convalescence following this procedure was uneventful, and the ureteral catheter was removed on the fifth postoperative day. No urine was passed through the urethra for the first ten days. Pyelograms following retrograde injection of an opaque medium into the ureter and kidney pelvis through the nephrostomy tube have failed to show any of the medium passing through the uretero-pelvic junction. (Fig. 10.) Attempts to dilate the uretero-pelvic junction from below have been unsuccessful, due to the tortuosity of the ureter. Although there has been a gradual increase in the amount of urine passed through the urethra, nephrostomy drainage is being maintained, in order to remove the burden of back pressure from the ureter and kidney. At no time has the urea nitrogen been above normal limits. The phenolsulphonephthalein function has increased, and the patient's general condition has improved.

A plastic operation on the kidney pelvis at a later date, with correction of the vesical neck obstruction, has been advised.

SUMMARY

1. Two cases of congenital malformation of the urinary tract with hydronephrosis, occurring in children, are presented.

2. In the second case there was bilateral congenital stricture at the uretero-pelvic junction, but there were no urinary symptoms. Early diagnosis in this case would undoubtedly have prevented the loss of one kidney and extensive damage to the other.

3. The first case presents a hypoplastic right kidney and hydronephrosis of the left kidney, with strictures at the uretero-pelvic and uretero-vesical junctions. The function of the hypoplastic kidney is insufficient to maintain life; therefore, the function of the other kidney must be preserved by establishing drainage.

SULFANILAMIDE AND PRONTOSIL IN THE TREATMENT OF HEMOLYTIC STREPTOCOCCUS EMPYEMA IN CHILDREN*†

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THE use of sulfanilamide and its derivatives in the treatment of infections due to the hemolytic streptococcus has been accorded an enthusiastic reception by the medical profession in the short time that has elapsed since the report by Long and Bliss.[1] The dramatic results from this form of chemotherapy, which have been reported by numerous investigators, foster the idea that it will cure such infections unless they are of utmost severity. Empyema due to the hemolytic streptococcus would seem to be an ideal field for the action of drug because the long time during which the fluid remains thin and can be removed by aspiration gives ample opportunity for the medication to forestall surgery, if that is possible. Our experience in this connection on the Children's Surgical Service at Bellevue Hospital has, however, been somewhat different.

Between January 1, 1937 and September 1, 1937 we have operated on twenty-three cases of empyema of which four were due to hemolytic streptococcus. These four cases were first treated on the Pediatric Service (Dr. Charles Hendee Smith, Director), and all received sulfanilamide, or its derivative, prontosil. During this period there were in Bellevue Hospital no other cases of empyema in children primarily caused by the hemolytic streptococcus, although in two cases that organism was a secondary invader in an empyema originally due to pneumococcus.

CASE REPORTS

CASE 1. G. C., white male, aged 10 weeks, was admitted to the Pediatric Service on March 3, 1937. Twenty-four days before this he had been in the hospital suffering from facial erysipelas for which he had been treated by prontosil. He had recovered promptly, but two weeks after discharge he developed cough and fever for which he was readmitted. On admission he had a well developed lobar pneumonia with pleural effusion. Aspiration of his chest yielded 200 c.c. of slightly cloudy fluid from which streptococcus hemolyticus was cultured. His temperature fluctuated between 104.4 degrees and normal for the first six days. On the sixth day 5 c.c. of prontosil was given intramuscularly three times, and thereafter twice a day. Meanwhile, the infant was put in an oxygen tent and given the standard treatment for pneumonia. There was no particular change in his course or temperature until the twelfth day when his temperature rose to 105 degrees and then dropped to normal by crisis. Meanwhile, since the baby had acquired a bright red color due to the prontosil, the drug was stopped for one day and then continued in 1 c.c. doses twice a day for eleven days. It was discontinued a week after the crisis as there was no longer any fever.

The fluid in the chest continued to accumulate and was aspirated about twice a week. It was almost clear at first, but soon became turbid and finally frankly purulent. In spite of this, the temperature remained normal after the crisis and on this account operation was deferred. However, the child's general condition became gradually worse, he developed a scoliosis, and, three weeks after the crisis, his chest

* *Author's Note.* Since this paper was written knowledge concerning sulfanilamide therapy has increased considerably, but our impressions about its application in empyema remain unchanged. When the causative organism of empyema is the hemolytic streptococcus, sulfanilamide therapy is indicated, but the indications for surgery are just the same as they were before the drug was introduced. Operation should not be deferred beyond the optimum time on the hope that chemotherapy will effect a cure alone.

† From the Children's Surgical Service, Bellevue Hospital, Fenwick Beekman, M.D., Director.

contained a considerable amount of pus which was too thick to run through the aspirating needle. Operation was now obviously necessary.

Under local anesthesia intercostal drainage with insertion of flapper tube was done thirty-two days after admission. Improvement commenced at once, but was slow. Except for the prolonged convalescence, the post-operative course was uneventful and the patient was discharged June 1, 1937 with wound healed and lung expanded.

Case II. R. B., a five year-old boy, was admitted to the Pediatric Service March 20, 1937. On admission he had a temperature of 104 as a result of lobar pneumonia and pleural effusion. Aspiration of the chest produced a clear fluid from which hemolytic streptococcus was cultured. Prontosil, 5 c.c., was given every four hours for four days, after which sulfanilamide was given in doses of 5 gr. three times daily. The routine treatment for pneumonia was also given. The temperature dropped to 100 degrees and fluctuated between this and 102 for ten days. It then rose to 104 and fluctuated around this level for another week. During this time the child's chest was aspirated nine times. The fluid, which was relatively clear at first, became cloudy and eventually purulent. On April 9, twenty days after admission, a rib resection was done and a flapper tube inserted.

The temperature dropped to normal after operation and did not rise to any extent thereafter. The discharge continued to be profuse, and sulfanilamide was therefore started again on the twenty-sixth post-operative day. There was no immediate effect from this treatment, but by the end of three weeks the hemoglobin had dropped to 65 per cent and the red blood cells to 2,500,000. The medication was then discontinued although there was still considerable drainage. Eventually the drainage ceased, the wound closed and the patient was discharged June 24, 1937 with lung expanded.

Case III. J. A., a two year-old boy, was admitted to the Pediatric Service March 8, 1937. He had been admitted to another hospital February 10, 1937 with pneumonia, and was subsequently transferred to Willard Parker Hospital as a diphtheria carrier. He developed bilateral acute otitis media during this time, and, when admitted to Bellevue from Willard Parker, had running ears on both sides and signs of consolidation in his chest. This was suspected of being fluid, but aspiration produced nothing. He was therefore treated for an unresolved pneumonia until it became evident that he had an encapsulated empyema. A second aspiration produced pus and rib resection was done at once. This opened an encapsulated, interlobar cavity, filled with pus and communicating with a bronchus. The cavity was packed with vaseline gauze. The immediate response to the operation was good, but on the second post-operative day the temperature went to 103. The packing was removed and replaced by a rubber tube allowing a large collection of pus to escape. On the same day the culture of pus taken at operation was reported as containing hemolytic streptococcus in pure culture. Sulfanilamide, 5 gr. every four hours, was ordered, but by the time the first dose was given the temperature was coming down, and before the second dose was given, had reached normal. It continued normal thereafter and the sulfanilamide was discontinued after two days, as it was thought the temperature fall was due to the reestablishment of drainage. The bronchial fistula closed spontaneously and the drain was removed twenty-three days after operation. Recovery was complete although the ears continued to drain for some time after discharge.

Case IV. H. P., a boy of 18 months, was admitted to the Pediatric Service June 6, 1937. He had been in another hospital since May 4, 1937 where he was admitted with bilateral acute otitis media, draining spontaneously, and lobar pneumonia. The pneumonia showed signs of resolution after two weeks, but then fluid appeared. The chest was aspirated May 31. The fluid was said to contain acid-fast organisms, for which reason he was transferred to Bellevue with the diagnosis of tuberculous empyema. On admission to Bellevue he had bilateral running ears, signs of an extensive collection of fluid in his left chest and a temperature of 102. Three hundred and fifty c.c. of slightly cloudy fluid was aspirated, from which a pure culture of streptococcus hemolyticus was grown. Careful examination of this and subsequent aspirations did not disclose any acid-fast organisms and two tuberculin tests were negative, as a result of which we concluded that the admitting diagnosis was erroneous. The child was immediately put on the routine treatment for pneumonia, two blood transfusions were given, and sulfanilamide was started. As he could not be induced to take the medication, he was given prontosil instead in doses of 5 c.c. every six

hours. The temperature fluctuated about the admission level of 102 for a week and then at about 103 and 104 for another week. Thereafter it dropped to normal, only to rise again five days later to 103. On June 25, sulfanilamide was substituted for prontosil in the original dose and this time it was readily taken.

Meanwhile the patient was subjected to repeated thoracenteses. The fluid which was thin and slightly cloudy on admission, became frankly purulent on June 25 and was too thick to run through the needle July 1. Cultures of the pus continued to be positive for hemolytic streptococcus and the general condition of the patient was becoming steadily worse. He was a very sick child when he was transferred to the surgical side on July 3.

Intercostal drainage under local anesthesia was done the same day and a flapper tube inserted. Improvement started at once. The drainage, which was profuse after operation, diminished as the baby improved and by July 22 was so scant that the tube was removed although he still had a slight amount of discharge from the sinus. Four days later he was transferred to Willard Parker Hospital as a diphtheria carrier. Upon his return to Bellevue, August 3, he had evidence of a re-accumulation of fluid in his chest. The tube was inserted again but no pus was obtained. He continued to do poorly, however, and his ears, though still draining as a result of chronic mastoiditis, were not considered sufficient cause for his trouble. On August 11, rib resection was done and a pocket of pus drained. A blood transfusion was given after operation and the patient began to improve at once. One week later sulfanilamide was started again, 5 gr. three times a day, in an attempt to expedite his recovery. It was discontinued two weeks later because of two unexplained temperature rises to 104. Shortly after this the tube was removed and the patient made a satisfactory recovery.

COMMENT

Of the four cases here reported three had adequate and prolonged treatment with sulfanilamide, prontosil or both. In these three cases a determined effort was made to control the disease by chemotherapy and repeated aspirations, but in all cases it required surgery to effect a cure. In the fourth case sulfanilamide was used late, after surgery had put the patient on the road to recovery. Incidently, this case had the shortest drainage time of the four and brought the average time from operation to final removal of drains to forty-five days instead of fifty-three days, the average of the three adequately treated cases. The other cases of empyema, in which organisms other than streptococcus hemolyticus caused the infections, averaged twenty-seven days of drainage.

On the other hand it is to be noted that none of the hemolytic streptococcus cases died, although three of them were very sick children, one of them only ten weeks old when admitted. Also, the temperature before operation was lower than would ordinarily be expected, a point to be remembered as it does not indicate resolution of the infection. Otherwise the course of the cases treated by chemotherapy was essentially that of the average case of hemolytic streptococcus empyema.

Sulfanilamide and its derivatives are useful drugs, but too much should not be expected of them. It is obviously unfair to draw conclusions from such a small series; however, we do call attention to the fact that in our hands hemolytic streptococcus empyema in children was not materially affected by chemotherapy and that adequate surgery is still necessary to effect a cure.

REFERENCE

1. Long, P. H., and Bliss, E. A. Para-amino-benzene-sulfonamide and its derivatives. *J. A. M. A.*, 108: (Jan. 2) 1937.

MULTIPLE FIBROUS LOOSE BODIES OF THE SHOULDER JOINT*

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CASES of loose bodies in joints are frequently reported in the literature, but so large a number as 800 loose bodies in the shoulder joint is not often encountered. The case here reported which came under our observation and which was operated upon, may therefore be worthwhile reporting. This case may also give a clue to the etiology of a condition that gives rise to such a multitude of bodies.

REPORT OF CASE

A. K., a housewife, 37, born in Austria, was admitted to Fordham Hospital on November 15, 1935, complaining of painful swelling of the wrists, left shoulder, left knee, and left ankle. The onset had been gradual and dated back two years.

The patient was married and had three healthy children, the youngest ten years of age. Her menstrual history was normal, and there was no history of previous diseases. She denied any venereal infection.

Physical examination disclosed a fairly well developed, middle-aged woman, slightly anemic. Heart and lungs were normal and gynecologic examination showed no abnormality. The wrists were swollen, but not red. Flexion and extension were distinctly limited, and crepitus was present. The left wrist was quite painful. The fingers were swollen at the proximal interphalangeal joints as in ordinary proliferative arthritis. The left shoulder showed marked swelling covering the entire aspect of the joint, extending down to the attachment of the deltoid. It was boggy in consistency, and one could feel the presence of fluid, but there was no tenderness. Motion was only slightly limited to abduction and outward rotation, but marked crepitus was present. The left knee was swollen and slightly tender at the medial side, but motion was only slightly limited. Crepitus was present. The left ankle was also swollen, and showed some spasm on motion.

Laboratory Findings. The blood count was normal, as was the urine. The vaginal, cervical and urethral smears were negative, and the blood Wasserman also negative.

X-ray of the left knee showed all the characteristics of hypertrophic arthritis, distention of the suprapatellar bursa, but no decipherable loose bodies. In the left shoulder a large, irregular, soft mass could be seen, but no bony irregularity. The joint space was normal. (Fig. 1.)

The shoulder was aspirated and 60 c.c. of amber-colored cloudy fluid was withdrawn. This was examined for malignant cells and organisms, neither of which were found. Guinea pig inoculation likewise gave a negative result, while the culture of the aspirated fluid showed no growth. The fluid was also injected intradermally, but no local reaction or wheal appeared.

An exploratory operation of the left shoulder was done on December 13, 1935. A semicircular incision was made on the left shoulder, with the convexity extending downward to the lower portion of the deltoid. The deltoid muscle, was markedly atrophied, and upon its cleavage, a large soft mass was found, which gave the impression of adhesions between the capsule and the lower portion of the deltoid and the acromion process. It was hard to find any pedicle. A syringe was put into the mass, but after many attempts, only 10 c.c. of straw-colored fluid could be removed. As it was impossible to shell out the mass, the capsule was opened and many small white pleomorphic soft masses were found. The head of the humerus was easily visible. The synovial membrane was thickened, irregular, and covered with some villi, not attached to pedicles. The

* Read before Fordham Hospital Alumni, October 5, 1936.

head of the humerus showed degeneration of the cartilage and some parts were covered with pannus. The loose bodies were removed. The pathologist later reported finding 671, but con-

Fig. 1. *X*-ray of the left shoulder before the operation.

sidering those that were lost on the operating table, the total number of these bodies was more likely about 800 (Fig. 2), some of which had been situated in the posterior aspect of the joint. It was evident that the masses had been in the capsule proper. The synovial membrane was removed where it was irregular, and a part of the capsule was also removed both for examination and to allow tight closure. The capsule was sutured in two layers.

The wound healed by first intention. The pain and swelling disappeared, and within ten days, the patient was able to use the shoulder freely.

Another *x*-ray taken later showed a clearer aspect of the shoulder joint. (Fig. 3.)

The patient was then discharged with instructions to return to the out-patient department for baking. The joint became normal both in contour and in function within six weeks, at the end of which time *x*-ray showed a perfect joint with good bone structure. (Fig. 4.)

Our diagnosis was a probable osteochondromatosis.

Pathologic Report. The specimen was carefully examined by the pathologist, L. R. Ferraro, M.D., who was kind enough to give us a detailed report for this publication. His statement was:

"*Gross:* Specimen consists of 671 joint bodies, ranging in size from a lentil to a small grape.

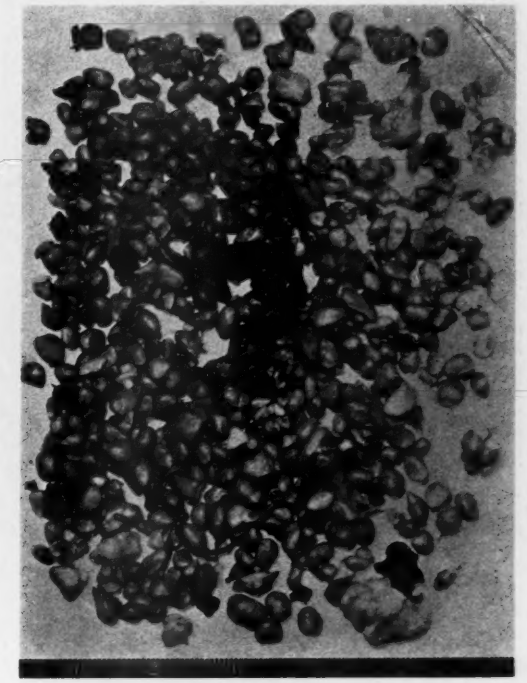

Fig. 2. The loose bodies removed from the shoulder joint.

The surfaces are smooth and glistening, with a greyish white color. They are of various shapes. Some are bean-shaped, others flattened; some are globular and a few are totally irregular. Cut section through many of these masses reveals an almost identical picture. This consists of a softer, translucent, pearly center and a thin cortical rim of denser white tissue. They all cut with little resistance; the cut surface resembles soft cartilage or coagulated albumin. Accompanying the specimen is a hemorrhagic fibrous capsule covered with a fibrinous exudate.

"*Microscopic:* Histologic sections were made from many of the joint bodies as well as from the pieces of capsule. The picture presented by the majority of the masses could be summarized as follows: The greater portion of the joint bodies consists of amorphous homogeneous pink-staining material in which a few scattered elliptical nuclei are noted. A number of small islands are also scattered throughout this area. These stain palely and occasionally present spindle-shaped nuclei. The periphery of the joint body contains definitely more cellular

elements. These consist of fibroblasts, lymphocytes and occasionally polynuclear cells. Small areas of nuclear débris are occasionally encountered. No cartilage or bone cells could be recognized in any of the sections.

FIG. 3. *X*-ray of the left shoulder taken five days after the operation.

FIG. 4. *X*-ray taken six weeks after operation, showing a normal joint.

"With azo-carmine stain, the greater portion of the body appears reddish in color, while at the periphery, irregular bands of collagenous bundles are noted. Sections through the capsule reveal dense areas of wavy collagenous bundles in which a number of small focal lymphocytic accumulations are found. The cellular reaction does not appear to be specific of any particular lesion. No synovial membrane could be recognized.

"*Diagnosis:* Multiple loose joint bodies; possible osteochondromatosis; chronic inflammatory reaction of the capsule."

The slides, together with the history, were sent to Dr. M. S. Henderson, who was kind enough to review the case. He also entertained the possibility of a diagnosis of osteochondromatosis, but as both our pathologist and the pathologist at the Mayo Clinic, Dr. Krenohen, found neither periosteum nor bone in the loose bodies, the diagnosis of osteochondromatosis was uncertain.

As the left knee was markedly swollen and the joint contour obliterated, we had the impression that there were loose bodies present. Accordingly, we decided to explore the joint as soon as the patient was able to undergo a second operation. *X*-ray of the knee showed ordinary findings of a degenerative arthritis, but no osteophytes.

On June 3, 1936, the knee joint was opened by a Krida incision. The synovial membrane was found markedly thickened with many large villi and polypi attached by small pedicles, but no loose bodies were found. A regular synovectomy was done and the specimen sent for examination. The wound healed by first intention. The patient had more use of the knee, and under continued treatment, the motion of the knee increased.

The specimen, again examined by Dr. Ferrara, was reported upon as follows:

"*Gross:* Specimen consists of the left suprapatellar bursa and a number of irregular pieces of synovial membrane removed from the left knee joint. On cut section the bursa presents a homogeneous appearance. There does not appear to be any other gross pathologic change. The synovial pieces of tissue vary in size from 1 to 5 mm. in length. From the edges of several of these pieces, a number of polypoid structures are seen to arise. These polypoid masses are pale brown in color, soft and edematous in appearance. Some of them present a short sessile attachment. Others have an elongated stalk. These polypoid masses vary in size from a split pea to a small cherry. The synovial membrane proper is definitely thickened and somewhat edematous."

COMMENT

As the synovial membrane showed distinct evidence of inflammatory changes, we feel that the changes in the shoulder joint were probably also originally inflammatory. The synovial membrane of the knee showed bodies attached with small pedicles. The same condition was probably present in the shoulder joint at the beginning so that the polypoid masses were the forerunners of the loose bodies. We feel justified, therefore, in considering the etiology of the case to be inflammatory.

CONCLUSIONS

1. A case of multiple fibrous loose bodies of the shoulder is reported. Almost 800 loose bodies found in the joint.

2. The synovial membrane of the knee showed many similar bodies, but with pedicle attached to the membrane.

3. The synovial membranes of both joints showed characteristics of chronic inflammation.

4. These loose bodies may therefore be inflammatory or infections in nature.

We wish to thank Dr. Ferraro for his examinations and careful study and Dr. M. S. Henderson for his review of the case.

REFERENCES

1. Henderson, Melvin S. and Jones, Hugh T. Loose bodies in joints and bursae due to synovial osteochondromatosis. *J. Bone & Joint Surg.*, 21: 400–424, 1923.
2. Mercer, Walter. Orthopedic Surgery. Wm. Wood & Co., Baltimore, 1936.

If treated early, the average compound fracture caused by indirect trauma is no more serious than a simple fracture.

NEW INSTRUMENTS

THE POSTERIOR HEEL (CALCANEAL) EXTENSION AND THE ANTERIOR TOE (EQUINUS) EXTENSION*

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PHILADELPHIA, PENNSYLVANIA

ONE of the causes of static weak feet in children is the presence of a congenital calcaneovalgus deformity. Occasionally, despite the wearing of Whitman weak foot braces (plates) and of balanced corrective shoes, the gait may remain awkward and the attitude in walking ungainly. The calcaneal heel is suggested as an aid in the further treatment of these patients. This device has also been used in the treatment of congenital and acquired, simple and compound, calcaneal deformities. It has been used in the treatment of mild paralytic calcaneal deformities to guide the growth of the foot and to aid in the restoration of the weakened calf muscles. The heel is extended posteriorly (Fig. 1) and by its fulcrum action tends to correct the usual heel gait of the patient with a calcaneal tendency.

FIG. 1. A, shoe with heel removed to expose the underlying upper. B, new heel extension and steel brace. C and D, shoe with posterior heel (calcaneal) extension.

* From the Orthopedic Service of the senior author at the Jewish Hospital, Philadelphia.

In making the posterior calcaneal extension, the heel of the shoe is removed to expose the underlying upper. A piece of leather is then attached, beginning at the breast of the heel where the sole was cut and extended beyond the shoe for a distance of one inch. (Fig. 1A and B.) A flat piece of steel, to act as a brace, is attached to the new heel to prevent bending when the shoe is worn. A top lift or heel is then applied. (Fig. 1C and D.) The height of the heel may be increased, if desired, to aid further in correcting the calcaneal attitude.

The anterior toe (equinus) extension is used in treating patients with equinus deformities without tendo Achillis contracture. It may be of value, therefore, in cases of mild spasticity of the calf muscle group and for the occasional child who walks on its toes without apparent cause. A short toe extension may also be of value in relieving the discomfort of patients with a hallux rigidus.

In making the anterior toe (equinus) extension, the sole and heel of the shoe are removed to expose the underlying upper (Fig. 2A) and a piece of leather is then attached to the sole, extending from the seat to 1 inch beyond the toe of the shoe. A piece of steel is incorporated, projecting to the end of the leather piece anteriorly. (Fig. 2B and C.) The heel and a new longer sole are applied. (Fig. 2D.)

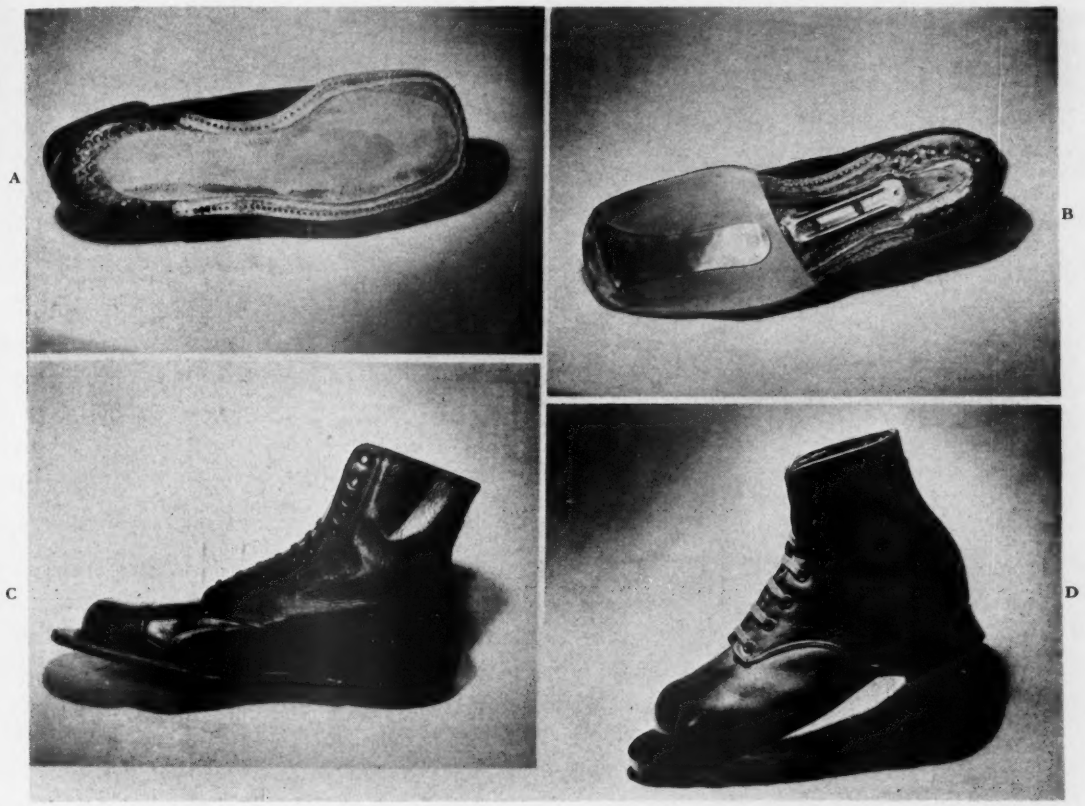

Fig. 2. A, shoe with sole and heel removed to expose the underlying upper. B and C, shoe with new sole extension and steel brace. Note brace extending from the posterior to the anterior surface of the sole, about one inch back from the toe of the shoe. D, shoe with anterior heel (equinus) extension.

SUMMARY

Two shoe corrections are described. Their purpose is to improve the attitude in walking of patients with calcaneus and equinus positions of the foot and ankle as previously described. They tend to make the gait more graceful. There is no awkwardness due to the extensions and the patients do not trip or fall.

[From Fernelius' Universa Medicina, Geneva, 1679.]

BOOKSHELF BROWSING

THE OPERATIVE STORY OF HERNIA

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THE year 1937 marked the fiftieth anniversary of Bassini's first contribution before the Italian Surgical Society, and the treatment of hernia as we know it today can properly be said to have begun with Bassini and Halsted. All attempts at cure before their time were ineffectual and, in the light of present knowledge, extremely crude.

Two examples of the many pre-Bassini-Halsted methods may be mentioned here: The first is that of McEwen who performed an extraperitoneal operation which consisted of making a pad of the unopened sac and fastening it up under the transversalis as far above the internal ring as possible. This was probably the best of the early operations but resulted in many recurrences. We still honor McEwen, however, by implanting the sutured peritoneum after excision of the sac as far superiorly as possible and call it McEwen's maneuver. The second pre-Bassini-Halsted operation, which is of interest, is that of McBurney, particularly because of the prominence of its author. McBurney opened the canal, sutured the sac as high as possible and then packed the canal with iodoform gauze, permitting it to heal by granulation. An extremely high incidence of recurrence resulted and the state of these patients was pitiable as cure by reoperation was impossible and the wearing of a truss uncomfortable. The results of this operation well illustrate the inability of scar tissue to act as a real supporting structure.

The most complete study of hernia prior to Bassini-Halsted was by Sir Astley Cooper, who wrote a book upon it in 1804. Little has been added to our anatomic knowledge of hernia since Cooper's book appeared and it is somewhat surprising that in spite of this eighty years elapsed before surgeons learned to cure hernia.

The present paper is an attempt to outline the various original procedures and contributions of lasting merit used in the treatment of inguinal and umbilical hernias. Many ingenious and useful modifications of these basic operations have been devised and are probably also worthy of study, but space does not permit their inclusion here.

Edward Bassini, the first name of importance, was born in Pavia, Italy, in 1844 and received the degree of Doctor of Medicine from the University of Pavia when only 22 years old. He became assistant to the Professor of Surgery at Pavia and at once showed an intense interest in anatomy and

surgical pathology. He followed closely the many new developments in surgery at that time and visited the clinics of Billroth in Vienna and Lister in London. He was one of the first Italian surgeons to practice aseptic surgery. In 1882 he was appointed to the chair of surgical pathology of the University of Padua. "He became Professor of Clinical Surgery in 1888 and he held this position until his retirement at the age of 75 in 1919. During this long and fruitful period, his epoch-making work on hernia appeared, as well as numerous other contributions to surgical literature. He was simple, almost austere in his tastes, of rigid moral fiber, a meticulous and cautious operator, and a kindly and interesting teacher. It is not surprising that he enjoyed the affection, as well as the admiration of his associates and pupils. He died in Verona, at the age of 80, on July 19, 1924."[1]

Fig. 1. Internal oblique and transversalis being sutured to Poupart's ligament. (After Bassini.)

Bassini studied the repair of the inguinal canal upon the cadaver before trying it upon a patient. In 1887 he reported the results of forty-two operations before the Italian Surgical Society, in 1888, reported 100 cases in one of the Italian journals, and in 1889 published a monograph "New Method of Operating for the Cure of Inguinal Hernia" which was printed by R. Stabilmento Prosperini in Padua. This last surveys minutely the results of 262 cases. The book consists of 106 octavo pages and contains four beautifully colored plates showing the technique used and the anatomic relations at the completion of the operation. In 1890 the results of 251 operations were reported in a German journal; outside of Italy little had been known of his work until this article appeared.

Fig. 2. Halsted's original operation. Sac has been excised and peritoneum closed. Cord has been reduced in size with remaining portion held aside. Interrupted sutures have been inserted and are ready for tying. (After Halsted.)

"Of the 251 cases, he followed all but four for periods ranging from one month to four and one-half years, itself a commendable achievement in clinical research. There were only seven recurrences in the total series of 251 operations (2.7 per cent), a record of which any surgeon of today could well be proud."[1] The technique of his operation is so well known that no description of it other than that shown in the illustrations will be attempted. The operation described by Bassini is being done today in hundreds of clinics throughout the world just as he performed it. It is doubtful if any other surgical procedure has received without alteration such universal acceptance.

Bassini also originated an operation for femoral hernia which is still extensively practiced. He excised the sac as high superiorly as possible and closed the canal with interrupted sutures uniting Poupart's ligament and the pectineal fascia.

William Stewart Halsted, the first Professor of Surgery at Johns Hopkins University, was born in 1852 and died in 1922. He was the son of a rich New York mer-

chant, a graduate in Arts from Yale College, and a graduate in Medicine in 1877 from the College of Physicians and Surgeons. After two years of study in Austrian and German clinics and eight years of teaching anatomy and practicing surgery in New York City, he went to Baltimore in 1889 as Chief Surgeon to the Johns Hopkins Hospital.

FIG. 3. Revised operation. Method of utilizing cremaster muscle. (After Halsted.)

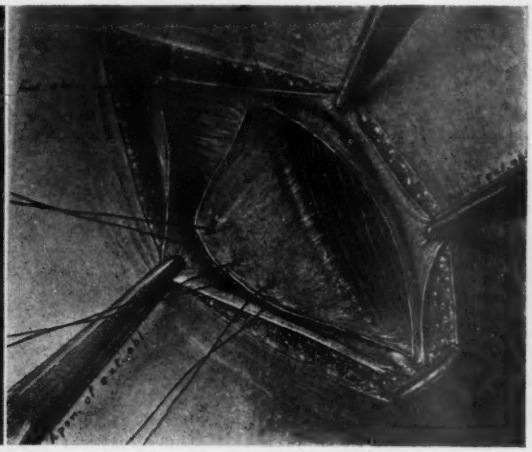

FIG. 4. Method of using rectus fascia strengthening repair of canal. (After Halsted.)

Time will not permit a complete recital of Halsted's contributions to the art and science of surgery. He was the first American surgeon to practice completely aseptic surgery. He introduced regional anesthesia and rubber gloves. He devised the first effective operation for cancer of the breast and independently of Bassini developed an operation for the cure of hernia.

Halsted's first operation was performed June 13, 1889 upon an 8 year old colored boy for a large congenital inguinal hernia on the right side. The sac when opened contained cecum and vermiform appendix. Upon November 4, 1889 before the Johns Hopkins Hospital Medical Society, Halsted presented an account of his first five cases. This was later reported in Volume 1 of the Johns Hopkins Hospital Bulletin. Halsted did not learn of Bassini's work until 1890 when it first appeared in German.

Halsted's operation differed in details but not in principle from Bassini's. His technique was as follows:

"1. The incision begins at the external abdominal ring, and ends 1 inch or less (less than 1 inch in children) to the inner side of the anterior superior spine of the illium on an imaginary line connecting the anterior superior spines of the illia. *Throughout the entire length of the incision everything superficial to the peritoneum is cut through.*

"2. The vas deferens, with its vessels, is carefully isolated up to the outer termination of the incision and held aside.

"3. The sac is opened and dissected from the tissues which envelop it.

"4. The abdominal cavity is closed by quilted sutures passed through the peritoneum at a level higher by 1½ to 2 inches than that of the so-called neck of the sac.

"5. The vas deferens and its vessels are transplanted to the upper outer angle of the wound.

"6. Interrupted, strong silk sutures, passed so as to include everything between the skin and the peritoneum, are used to close the deeper portion of the wound, which is sewed from the crest of the pubes to the upper outer angle of the incision. The cord now lies superficial to these sutures, and emerges through the abdominal muscles about one inch to the inner side of the anterior superior spine of the illium.

"7. The skin is united over the cord by interrupted stitches of very fine silk."[15]

The first cases were drained with gauze, but this was soon abandoned and the wounds closed without drainage. At first

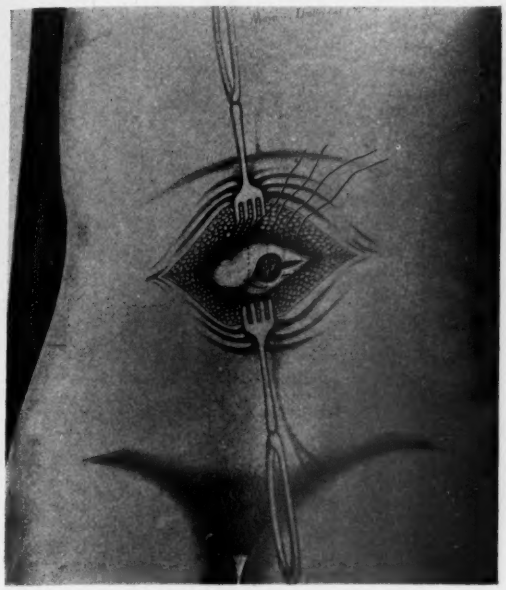

Fig. 5. Overlapping method of repairing umbilical hernia. (After Mayo.)

Halsted laid great stress upon transplantation of the cord and reduction of the size of the cord by excision of some of its veins. Transplantation was later considered unnecessary and venous excision was abandoned because of resultant testicular atrophy in some cases.

In his final modification Halsted no longer used the through-and-through sutures; instead he utilized the cremaster muscle to reinforce the internal oblique and transversalis. The internal oblique was then sutured to Poupart's ligament and the external oblique closed by imbrication. He considered the most important part of his operation the wide exposure with high ligation of the sac. I believe that most of the poor results today are primarily due to failure to follow the principles taught by Halsted in his first paper. Unquestionably the most important of all is high suture of the sac.

After 1890 Bassini made few if any additional contributions to the study of hernia while Halsted continued to study the subject and made nine separate printed contributions, the last one of which was prepared in August 1922 and appeared after his death. In his last article he made

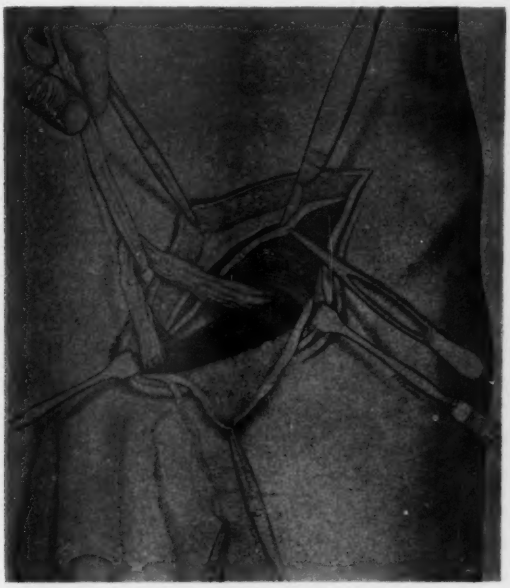

Fig. 6. Method of obtaining autoplastic sutures. (After McArthur.)

the following statement: "There is not in any language a study of the ultimate results or of the relative importance of the various details of the operation comparable to ours." Both Bloodgood and Taylor made valuable studies of the Halsted material and results and Cushing, of the Halsted clinic, was probably the first to perform the operation with local anesthesia.

The second of Halsted's longer papers, "The Cure of the More Difficult as Well as the Simpler Inguinal Ruptures," which appeared in the Johns Hopkins Hospital Bulletin for 1903, gave illustrations of his modification of his original operation. Here too is an account of his transplantation of the rectus sheath for the larger direct hernias. This maneuver was also done independently by a French surgeon named Berger.

In practically all of his operations Halsted used sutures of fine silk. His studies of the reaction of wounds to different suture materials were extensive and thorough and he used the fine silk sutures because of a higher percentage of primary healing and better final results. Wangen-

steen[12] has recently made the following statement relative to silk sutures: "I am inclined to believe that the silk sutures

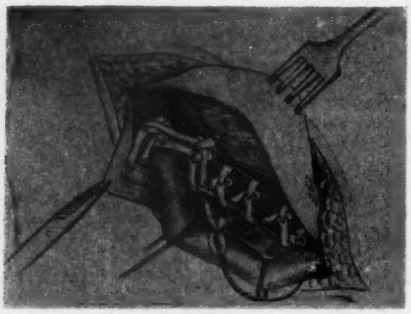

Fig. 7. Fascial sutures in repair of hernia. (After Gallie.)

which Kocher and Halsted employed and recommended are an important item in the surgical repair of hernia. I believe that surgeons will employ them with increasing frequency." In his last paper upon hernia, Halsted stated that he had not had a recurrence in over twenty years.

After Bassini, the cure of hernia is entirely an American contribution. The second American to distinguish himself in this field was W. J. Mayo who was born at New Ulm, Minnesota, and who has practiced surgery in Rochester, Minnesota since 1883. Prior to Mayo's studies, efforts to cure umbilical hernia were directed toward covering the defect with muscle. Failure followed in almost all cases and until his time umbilical hernia was considered a hopeless condition.

Mayo's first operation was performed in 1895 and consisted in overlapping, from side to side, muscle and the aponeurotic structures which compose the neck of the hernia. Later he found that overlapping of fibrous structures only from above downward was preferable. In his first report he covered five cases. His description of how he first used the above downward overlapping is interesting.[6] "This method we had then employed in five cases: in three the overlapping was from side to side, and in two from above downward. Extensive lateral incisions to find sufficient muscle to make the routine operation described by surgical writers compelled us, as a matter of necessity, to overlap from above downward in these two cases and, to our satisfaction, we found the parts came together

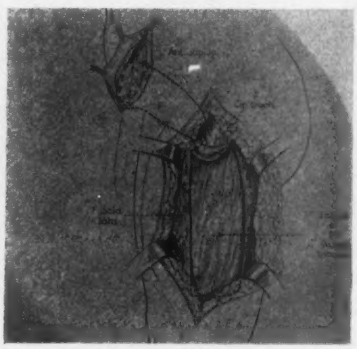

Fig. 8. Transplantation of fascia with pedicle. (After Wangensteen.)

with less tension than when drawn laterally, and time proved that the strength of union was as lasting."

In addition to being the most widely accepted method of treatment of umbilical hernia, the principle of Mayo's operation is utilized in treating post-incisional and other forms of ventral hernia.

The next original contribution of lasting merit was by Lewis L. McArthur of Chicago. McArthur was the first to use fascial sutures, the strips of fascia being obtained from the split aponeurosis of the external oblique. McArthur made a preliminary report in 1901 before the Chicago Surgical Society, and a subsequent report covering eighty-five patients in October 1904 in the Journal of the American Medical Association. McArthur reported no known recurrences in the eighty-five patients, eight of them having bilateral repairs. The technique of McArthur's operation is clearly shown in his illustrations. He noted that his method was equally adaptable to the Bassini, Halsted and other procedures.

In 1909, Kirschner demonstrated the feasibility of using free transplants of fascia lata for various operations. These transplants were used as substitutes for dura and tendons, for reinforcements of tendons, as substitutes for articular ligaments and other operations.

In 1921, W. E. Gallie and A. B. LeMesurier of Toronto, dissatisfied with their own and other surgeon's results in large, direct and recurrent hernias, went a step further than McArthur and Kirschner and used free transplants of strips of fascia lata. Their clinical work was predicated upon a series of carefully executed experiments. Studies were made of the effects of catgut, silk, and fascial sutures when inserted into the supporting structures of animals. They demonstrated experimentally that supporting structures sutured with autogenous free strips of fascia were much more strongly united than when sutured with catgut, linen or silk.

Gallie's results with this method have been excellent indeed, particularly so since practically all of his operations have been for extremely large primary or recurrent hernias. Their method is used for inguinal, umbilical and ventral hernias. In 1930 Gallie[11] reported a series of 200 cases with only six failures, although "among them were ventral and inguinal hernias so enormous as to be almost unbelievable." Gallie's method has received wide approval and acceptance by other surgeons.

James C. Masson[13] made the following statement of his experience: "During 1936 we used living sutures in the repair of hernia in 145 cases. Some of them were huge postoperative hernias and the others were either direct or recurrent inguinal hernias. Altogether we have used fascia lata transplants in about 745 cases of postoperative or inguinal hernias."

The strips which Gallie uses are cut from the fascia lata through incisions in the lateral surface of the thigh. They are one-fourth inch wide, the length varying with the needs of the individual case, some of them being as long as 10 or 12 inches. Gallie sutures the defect in the thigh. Some surgeons have devised instruments for cutting the fascial strips through small puncture wounds and leaving the defect unsutured. In his papers upon hernia, Gallie has insisted, and properly so, that supporting structure must be united to supporting structure without intervening areolar or other tissue.

In 1931, after removing a large desmoid tumor from the left lower abdominal wall in a young woman, Wangensteen found the resulting defect so great that he was unable to close it by approximating the residual tissues. The opening seemed to be too large to close with woven free strips of fascia lata so "the plan of employing the iliotibial tract as a pedicled graft on the tensor fascia lata muscle suggested itself as a feasible procedure."[14] The results were so satisfactory that he subsequently used the method with success in recurrent and large hernias of all types.

After exposing the defect in the abdominal wall, Wangensteen makes a long elliptical incision in the thigh and raises a large flap of fascia lata with the pedicle composed of muscle tensor fasciae latae. The flap is then sutured into or across the defect. In repairing inguinal hernias, Wangensteen carries the flap anterior to Poupart's ligament, but for incisional hernias it is brought posterior to the ligament. The defect remaining in the thigh has not resulted in any disability. Wangensteen's operation has not been used sufficiently by other surgeons to determine properly its indications and value, but as it is based upon sound surgical principles it has real merit. There is no doubt that it will be of definite usefulness in the treatment of very large hernias.

CONCLUSION

As previously stated, many modifications of technique in treating hernia have been omitted in this paper. It is believed, however, that the principles of treating hernias have been presented. We can agree with Halsted, whose last written words upon the subject were, "The cure of hernia may be listed with the triumphs of surgery."[5]

REFERENCES

1. Zimmerman, Leo M., and Heller, Richard E. Edoardo Bassini, his role in the development of hernial surgery. *Surg., Gynec. & Obst.*, 64: 971–973 (May) 1937.

2. Coley, W. B. Review of radical cure of hernia during the last half century. *Am. J. Surg.*, 31: 399–402 (March) 1936.
3. Halsted, W. S. The radical cure of inguinal hernia in the male. *Bull. Johns Hopkins Hosp.*, 4: 17–24, 1893; *Ann. Surg.*, 17: 542–556, 1893.
4. Halsted, W. S. The cure of the more difficult as well as the simpler inguinal ruptures. *Bull. Johns Hopkins Hosp.*, 14: 208–214, 1903.
5. Halsted, W. S. An additional note on the operation for inguinal hernia. Surgical Paper, The Johns Hopkins Baltimore Press.
6. Mayo, W. J. Further experiences with the vertical overlapping operation for the radical cure of umbilical hernia. *J. A. M. A.*, 225–228 (July 25) 1903.
7. McArthur, Lewis L. Autoplastic sutures in hernia and other diseases. *J. A. M. A.*, 10–39–1048 (Oct. 8) 1904.
8. Gallie, W. E., and LeMesurier, A. B. Living sutures in the treatment of hernia. *Canad. M. A. J.*, 13: 469–480 (July) 1923.
9. Gallie, W. E., and LeMesurier, A. B. The use of free transplants of fascia as living sutures in the treatment of hernia. *Arch. Surg.*, 9: 516–529 (Nov.) 1924.
10. Gallie, W. E. Closing very large hernial openings. *Ann. Surg.*, 96: 551–554 (Oct.) 1932.
11. Gallie, W. E., and LeMesurier, A. B. The late results of the living suture operation in ventral and inguinal hernia. *Canad. M. A. J.*, 23: 165–168, 1930.
12. Wangensteen, Owen H. Personal communication.
13. Masson, James C. Personal communication.
14. Wangensteen, Owen H. Repair of recurrent and difficult hernias and other large defects of the abdominal wall employing the iliotibial tract of fascia lata as a pedicled flap. *Surg., Gynec. & Obst.*, 59: 766–780 (Nov.) 1934.
15. Halsted, W. S. The radical cure of hernia. *Bull. Johns Hopkins Hosp.*, 1: 12–13, 1890.
16. Bassini, Edoardo. Nuvo metodo operativo per la cura dell'ernia inguinale. Padova, 1880. R. Stablimento Prosperini.

Compound fractures from direct trauma are far more serious and radical measures are necessary if sepsis is to be avoided and the limb saved.

The fillers in this issue are from "Experience in the Management of Fractures and Dislocations" by the Staff of the Fracture Service, Massachusetts General Hospital (Lippincott).

SPECIAL ARTICLE

The Rôle of the Electrical Potential of Cells and Tissue Fluids in Normal and Pathologic Metabolism

A Guide to Rational Preoperative and Postoperative Therapy

BY

RUDOLF KELLER, Ph.D.

AND

EDWARD SINGER, M.D.

AMERICAN JOURNAL OF SURGERY, Inc.

NEW YORK • MCMXXXIX

THE ROLE OF THE ELECTRICAL POTENTIAL OF CELLS AND TISSUE FLUIDS IN NORMAL AND PATHOLOGIC METABOLISM*

A GUIDE TO RATIONAL PREOPERATIVE AND POSTOPERATIVE THERAPY

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PRAGUE, CZECHOSLOVAKIA NEW YORK CITY

ELECTRICAL phenomena were examined in electrically charged submicroscopic (colloidal) and amicroscopic (ionized) particles. This paper is devoted to a study of the electrical phenomena that occur in microscopic dimensions, that is in cells, and to the behavior of molecules which migrate in the cells. As the surface potentials of non-electrolytes play the most important rôle here, the discussion will be largely about the electrokinetic potential, the ζ potential† of Freundlich.[11] Although the magnitude of this potential is only about 1/100,000 of the potential with which one deals in ionic chemistry, it is a basic factor in all biologic occurrences and is fundamental in cellular metabolism.

The importance of the electrical potential in cell metabolism has been suspected for some time, but careful and exact investigation of this problem has been possible only in the last decades. We have only recently achieved sufficient perfection in micromethods to enable us to measure electrical currents of a few microvolts and microamperes in single living cells. For the development of the methods available for this investigation American research workers are largely responsible. Chambers[3] devised the first micromanipulator. The electrical potentials of single nerve cells and muscle cells were measured by Lillie[26] and Gasser,[14] those of algae cells by Osterhout,[34] Blinks[2] and Irwin[18] various parts of plants by Lund,[28] Marsh,[29] and Rosene,[40] and the unfertilized and fertilized ova by Gelfan.[15] Besides actual measurements vital staining was also used to discover the electrical potential of cells, and Singer[44–50] described the electrical potential of kidney and suprarenal cells based on experiments with fluorescent vital staining.

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† The potential difference represented between the potential of a fluid adherent to a solid wall against the movable fluid in the inside. This potential difference is dependent upon the nature and concentration of the substances dissolved in the fluid.

It is necessary to include the results of the investigations of these authors and other information from the literature in order to arrive at a more general conclusion than would be possible to on the basis of our findings alone. The experimental data already published are of real significance and when correctly coordinated supply further evidence for our interpretation. As a matter of fact a critical reëxamination of findings already recorded from the aspect of electrical structure forms an essential part of this work. The electrical structure of the various organs will be described and compared with their optical and mechanical structure. Thus a normal and pathologic electrohistology will be given.

METHODS OF INVESTIGATION

Conclusions to the electrical structure of organs can be made by vital staining. Vital staining with fluorescent dyes is especially useful and laws governing color appearance are systematized in Table 1.

The results of the vital stainings are controlled by reëxamination with the multielectrodes of Nistler.[31] These two methods of examination supplement each other, as both have inherent errors that one can not easily eliminate. Negatively charged particles penetrate easily into normal cells, while positively charged particles can be introduced only with difficulty for the most part. The results of vital stainings are therefore displaced in the positive direction. This error is even greater with the ordinary daylight visible dyes. In measurements with micro-electrodes the error is in the opposite direction. The positive granuli and membranes are in many cases smaller than the finest micro-electrodes and therefore the surrounding negative plasma substance is measured, at least in part, with them. Accordingly micro-electrical measurements are displaced towards the negative direction.

INTERRELATIONSHIP BETWEEN ELECTRICAL POTENTIAL AND MINERAL (RESIDUAL ASH) AND ORGANIC CONTENT OF ORGANS

According to their electrical charge, organs contain various minerals and organic substances. Therefore, the mineral content is characteristic of the physiologic and pathologic states of organs and of the entire organism. A definite alignment is manifested between the positive sodium group and the negative potassium group in the positively and negatively charged organs. Various members of these

antagonistic groups were described by Jacques Loeb,[27] who was the first to notice this antagonism and who called attention to the counter-effect of NaCl to poisoning with KCl.

TABLE 1

VITAL STAINING WITH FLUORESCENT SUBSTANCES

THE DECISIVE FACTORS FOR THE STAINING ARE THE PHYSICO-CHEMICAL PROPERTIES OF THE FLUORESCENT DYES AND THOSE OF THE LIVING TISSUES.

I THE PHYSICO-CHEMICAL PROPERTIES OF THE COLOR PRODUCING SUBSTANCES:

A. THE ELECTRIC CHARGE POSITIVE DYES ARE ATTRACTED BY NEGATIVE TISSUES AND VICE VERSA. THE CHARGE IS UNSTABLE ON MOST OF THE COLOR PRODUCING SUBSTANCES AND VARIES IN THE SAME ELECTRIC FIELD ACCORDING TO

1 CONCENTRATION in diluted solutions particles are adsorbed by the serum colloids of opposite charge and take the charge of the colloid

2 pH not highly dissociated acid and alkaline fluorescent dyes change their charge according to the electric field in which they travel

3. SIZE OF THE PARTICLES IN THE DISPERSED PHASE
- a. coarse dispersed 0.1mm-500mμ
- b. colloid dispersed 500mμ-1mμ
- c. highly dispersed <1mμ

B. SIZE OF THE PARTICLES IN THE DISPERSED PHASE OF THE COLOR PRODUCING SUBSTANCE WILL INFLUENCE THE DIFFUNDIBILITY

C. CHEMICAL AFFINITY

D. OXIDABILITY AND REDUCIBILITY

E SURFACE DYNAMIC ACTION OF THE PARTICLES

II THE PHYSICO-CHEMICAL PROPERTIES OF THE LIVING TISSUE

A. THE ELECTRIC CHARGE POSITIVE TISSUE ATTRACTS NEGATIVE DYES AND VICE VERSA

B. MECHANICAL STRUCTURE AND TRANSMISSION DENSITY THIS MAKES IT POSSIBLE OR IMPOSSIBLE FOR THE SUBSTANCE TO TRAVEL TO DIFFERENT PLACES OF ATTRACTION DIFFERENCE IN STAINING ACCORDING TO THE MANNER OF APPLICATION

C. pH ALKALINE POSITIVE WILL NEGATIVIZE THE ELECTRICALLY UNSTABLE FLUORESCENT SUBSTANCES ACID NEGATIVE WILL POSITIVIZE THE ELECTRICALLY UNSTABLE FLUORESCENT SUBSTANCES AT THE ISOELECTRIC POINT THERE IS NO STAINING

VITAL STAINING IS NOT GOVERNED BY THE FOLLOWING CHARACTERISTICS OF THE COLOR PRODUCING SUBSTANCES

I. ACIDITY OR ALKALINITY IN DISTILLED WATER THE RELATIVE ACIDITY OR ALKALINITY CHANGES ACCORDING TO THE ISOELECTRICAL NIVEAU OF THE GEL MEMBRANES IN THE LIVING CELLS.

II. CHEMICAL CONSTITUTION CHEMICALLY CLOSELY RELATED SUBSTANCES BEHAVE DIFFERENTLY AND SIMILARLY ACTING SUBSTANCES BELONG TO A VARIETY OF CHEMICAL GROUPS.

III. SOLUBILITY IN LIPOIDS NOT DISSOCIATED (NON IONIZED) MOLECULES PENETRATE LIVING CELLS EASIEST LIPOIDS AND OTHER SOLVENTS, KAOLIN, CHARCOAL, ETC., WITH LOW DIELECTRIC CONSTANT SEEM TO HAVE A SPECIAL AFFINITY TO THESE SUBSTANCES WHICH WATER WITH HIGH DIELECTRIC CONSTANT DOES NOT HAVE. LACK OF DISSOCIATION NOT LIPOID SOLUBILITY IS IMPORTANT.

1. blood serum, lymph, tissue and cell fluids secretions
2. phase designates the parts of a substance that are separated by physical means. dispersed, internal, phase is the aggregate of finely divided suspended particles in a colloidal solution
3. inductivity of a non-conductor.

According to Loeb's interpretation an antagonism exists not between two ions of opposite charge but between ions of the same charge. The riddle created by this important discovery was solved by the recognition, that the effect is not caused by "ion antagonism." Ionized potassium migrates in the electric field in the same direc-

tion as ionized sodium. The antagonism is, however, between the positive ions of sodium and the (in organic compounds) non-ionized potassium complexes.

Tisdall,[52] Gamble,[13] and Fenn[7] also found that minerals migrate in two antagonistic groups. Nearly all members of these two antagonistic groups were discovered by Wertheimer,[56] who proved, by using a frog's skin as membrane, that K, Mg, NH_4, glucose, and basic dyes (negative group) migrate from inside to outside; while water, Na, Cl, amino acids, salicylates, rhodanide, and acid dyes (positive group) migrate from the outside to the inside. Keller[21] and his co-workers tested these substances in the high tension apparatus of Fürth[12] in presence of an overplus of biologic colloids, which adsorb one or the other. They found that K, the potassium group, was negative, and Na, the sodium group, was positive.

Therefore a study of these groups will give us clues to electrical phenomena in the organism where at present direct measurements are impossible. (Table II.) The alignment of these groups in the

TABLE II

ANODIC SUBSTANCES IN BLOOD PLASMA

(Negatively charged in blood plasma)

Basic Dyes:

Methylene blue, neutral red, methyl violet, chrysoidin, acriflavine, safranine, malachite green. (In distilled water these dyes are positively charged.)

Acid Dyes:

Congo red (coarsely dispersed), trypan blue, isamine blue. (In section these dyes act positively charged.)

Other Substances:

Glucose, urea, cholesterin, uric acid, creatinine, ammonium salts, potassium salts, sulfates, phosphates, insulin, gluthatione, non-dissociated calcium and non-dissociated magnesium, iron, iodine, silver salts, manganese, cobalt, arsenic, India ink, hormones, vitamins (with the exception of vitamin C).

CATHODIC SUBSTANCES IN BLOOD PLASMA

(Positively charged in blood plasma)

Basic Dyes:

Hematoxylin

Acid Dyes:

Fluorescein, uranin, eosin. (In distilled water these dyes are negatively charged, but in section positively.)

Other Substances:

Water, chloride, bromide, salicylic acid, rhodanide, esculin, vitamin c, sodium.

normal organism can be seen from Fig. 1, which shows that in comparison with the average content of the organism as a whole, the negatively charged organs have an excess in water and in the Na group, and a deficit in the K group, while the positively charged organs show the reverse condition.

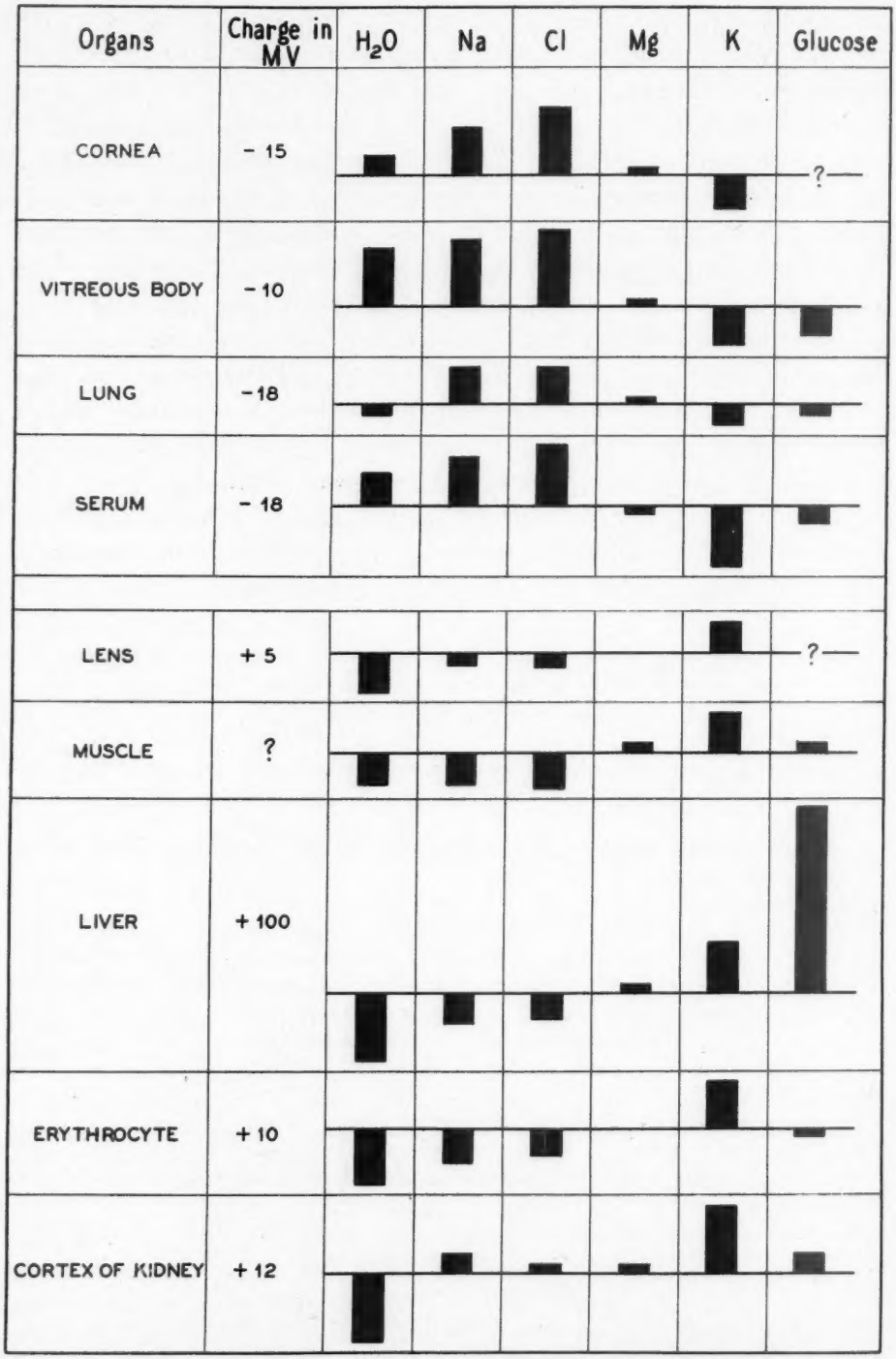

FIG. 1. The negatively charged organs have an excess in water and in the sodium group and a deficit in the potassium group, while the positively charged organs show the reverse condition in comparison to the content of the whole organism in these groups.

THE ELECTRICAL POTENTIAL OF VARIOUS ORGANS

THE LIVER

The electrical potential of the liver cells was first examined by Okuyama[33] who measured the oxidation reduction (redox) potential with gold electrodes and found that the liver parenchyma cells had 100 to 150 millivolt positive tension. Gicklhorn[17] Kaunitz and Schober,[20] Dejdar,[5] and Nistler[31] found by measuring with egg albumin micro-electrodes that the potential of the parenchyma cells of the liver of frogs and salamanders had a positive tension of only 25 to 30 millivolts. Since measurements with micro-electrodes give only rough, quantitative results and the numerical outcome depends greatly on the methods applied, one can understand the numerical difference between Okuyama's and other experiments. The significant point in these experiments is, however, not the numerical result, but the sign of the potentials. All investigators who have measured the potential of the liver parenchyma, have found it positive. Vital stainings with dyes that are visible in ordinary light and with dyes that are fluorescent have confirmed these findings. Thus as far as a qualitative analysis is concerned, the liver has parenchyma cells with strongly positive protoplasm. Quantitative estimation of the results varies, but lower figures were found by the majority of investigators. We shall therefore accept in our calculation the lowest figures as correct.

As these potentials exist in distances of 0.002 mm. between the positive parenchyma cells and the negative bile capillaries (potential 20 millivolt negative), the potential difference per centimeter is 425 volts. The liver is therefore a real high tension apparatus.

The highly positive charge is characteristic of the normal liver parenchyma cells. These cells, however, are storage places for biologically electro-negative substances, such as glucose, glycogen, phosphates, urea, potassium compounds, a majority of the vitamins, and basic dyes. These substances are attracted, while the biologically electro-positive substances, such as water, sodium chloride, amino acids, and acid dyes are energetically repelled.

In various pathologic conditions the electrical charge of the liver parenchyma becomes lowered. The parenchyma cells lose the ability to attract negatively charged substances and to repel positively charged ones, with the result that the storage of potassium, glucose, and phosphates is diminished and the content of sodium and water increases. When this occurs acid dyes are able to enter

the liver parenchyma, as was demonstrated by Roller and Schober. When uranine is injected into an animal with normal liver, this acid dye appears in the vessels of the liver and in the bile capillaries,

FIG. 2. The superficial veins of the liver in fluorescent light of uranine.

FIG. 3. The same area as in Figure 2 after poisoning with allyl formiate, showing typical accompanying band (Begleitstreifen).

but the parenchyma cells do not show it. By injection of allylformiate Roller and Schober[38] were able to depress the electrical charge of the parenchyma within a few minutes and could make the liver edematous. Uranine then entered the parenchyma cells along the blood capillaries and formed a luminous band (Begleitstreifen) bordering them. (Figs. 2 and 3.)

A fall in the electrical potential of the liver parenchyma can also be observed after various other poisonings, after severe operations, blood loss, and impairment in circulation. It might also be caused by lack of oxygen, fever, chronic diseases, and diphtheria toxin.

Kaunitz[19] observed in his analysis of residual ash of livers of guinea pigs a loss in the biologically negative potassium group during the effect of low oxygen pressure, poisons and diseases; but changes that for themselves could be used for interpretation were not evident from the figures of the biologically positive sodium group. It becomes clear, however, by the calculation of the molecular K/Na ratio,

that there was in every case a relative displacement of K in favor of Na. (Table III.) On the other hand drugs of the pyramidon, digitalis, and strophanthin groups increased the potential of the liver parenchyma above normal.

TABLE III

AVERAGE POTASSIUM AND SODIUM CONTENT OF GUINEA PIG LIVERS

Diagnosis	No. of Animals	K—mg. Per Cent	Na—mg. Per Cent	K/Na Molecular Ratio
Normal	32	273	134	1.19
Diphtheria toxin	6	234	135	0.99
Urea poisoning	3	121	79	0.89
Cholesterin poisoning	2	181	130	0.82
Allyl formiate poisoning	2	116	234	0.30
Low oxygen pressure	19	167	126	0.76

The results of various types of research work done on the liver indicate that the electrical potential of the liver parenchyma reflects the physiologic or pathologic state of the cells.

THE ERYTHROCYTES

Normal erythrocytes contain a large amount of negatively charged substances, such as glucose, glycogen, urea, potassium lactate, phosphates, etc., and accumulate basic dyes. The storing of these substances is caused by the positive charge of the principal parts of the erythrocytes. Some parts of the erythrocytes, however, have a negative charge according to Gicklhorn's[17] observations. He could stain a thin membrane around the erythrocytes of the salamander by the acid dye uranine. A framework within the erythrocytes appeared also. Keller[22] and Singer[51] could not observe any staining in the membrane of red blood corpuscles that were in the blood stream of capillaries. Singer observed after the application of acriflavine only a staining, which appeared in the nuclei of the red blood corpuscles of the frog. A failure to produce staining, or more correctly in this case, a lack of fluorescence, might be due, however, to the filter effect of hemoglobin to the ultra-violet rays.

The erythrocytes of the salamander are relatively large (55μ in diameter) and therefore Gicklhorn was able to measure their outer membrane against their inner parts with an electro-potential meter. The results of these measurements were in accord with the vital staining. They disclosed that the outer membrane was 10 to 11 millivolt negative in comparison to the inner parts.

Seki[42] came to a similar conclusion by measuring the charge of the erythrocytes by an entirely different method, namely by their cataphoresis. He saw the erythrocytes migrating to the anode. The velocity with which the erythrocytes migrated in the electric field, however, varied not according to the size of the erythrocytes (Lamb's[25] law) but independently of it, according to the species of the animals from which blood was obtained. The velocity for the dog was 1.7μ for the cat 1.5μ, for man 0.9μ, and for the rabbit 0μ, per second. He called attention to the fact that cataphoresis reveals only the potential difference between the surface of the cell and the surrounding fluid; the inside potential of the cell has no effect on it. His staining experiments, however, indicated that the inside of the erythrocytes has a positive potential. Independently of Gicklhorn he concludes from his cataphoresis experiments, that the erythrocytes are surrounded by a differentiated outer layer or membrane, which is formed by a negatively charged substance. The gradient of the electrical charge, which the erythrocytes of the various animals possess, depends upon substances that imbibe the membrane. He first thought the substance might be a lipoid, later he came to the conclusion that it might be an individually different hemoglobin. The analysis of the mineral contents of the erythrocytes, however, suggests an entirely different reason for the variation in the electrical charge. The sodium and potassium content of the erythrocytes of these animals is shown in Table IV. Taking the

TABLE IV

SODIUM AND POTASSIUM CONTENT OF ERYTHROCYTES IN MAN AND ANIMALS

	Dog	Cat	Man	Rabbit
Sodium	0.28	0.27	0.1	0.13
Potassium	0.02	0.02	0.33	0.43

figures of this table into consideration, the gradient of the electrical charge of the erythrocytes is parallel with their potassium and sodium content. As for the glucose, urea, fat, and lecithin content, one would expect a higher amount, but other minerals confirm the group rule. We may conclude, that for erythrocytes the different methods used by the various investigators, vital staining, mineral analysis, fluorescence by ultra-violet light, and measurements by micro-electrodes and cataphoresis gave the same results.

MUSCLE

Experiments for the determination of the electrical charge of the intact muscle meet with such difficulties and the results are often

so contradictory that their validity has to be questioned. One of the reasons is that muscle tissue is extremely sensitive to manipulations. Injuries that are not perceptible to the naked eye cause a typical injury or cathode current. Vital staining is also difficult. Some staining was obtained with negatively charged dyes, but they stained only granules. On the mineral metabolism, however, we possess exact data.

Fenn[7] found that muscle during action loses potassium and increases its sodium content. This phenomenon is characteristic of nearly all organs. His figures on the average electrolyte changes in the rat gastrocnemius muscle during stimulation can be divided into two characteristic groups. (Table v.) The negative group,

TABLE V

ELECTROLYTE CHANGES IN RAT MUSCLE

(Concentration in millimolls per 100 gr. dry weight)

		Average Content	Change in Stimulation	Change in Recovery
Negative	K	47.3	− 6.1	+ 3.6
Positive Group	Na	7.6	+ 8.3	− 6.4
	Cl	5.4	+ 2.8	− 2.0
	H_2O	318	+49	−43

represented by potassium, leaves the muscle, and the positive group, represented by sodium, chlorine, and water, enters into it. Kaunitz in some unpublished analyses obtained somewhat similar results. From inference we may conclude that muscle has a positive charge, which becomes depressed by fatigue or exhaustion and which will be resumed or restored by rest.

NERVOUS TISSUE

On the basis of his studies in fresh frozen sections, Unna[54] described nervous tissue as a place of reduction. A site of reduction is equivalent to a cathode. (Reduction takes place at the cathode.) Kreibich's[24] experiments on living objects with rongalit white revealed that nervous tissue is a site of oxidation, which is identical with the anode or a place of positive charge. Gicklhorn and Keller[23] were able to demonstrate that nerve tissue can be the site of either reduction or oxidation in the same animal, depending upon its functional state. Thus both Unna's and Kreibich's statements are correct.

Organic specific vital staining of sensory nerve fibers was accomplished by means of diluted methylene blue in cocaine in daphnia.[23]

The dye appeared first in the nine rods of the peripheral organ, hypothetical taste organ (Riechstäbchen) of the animal. From the rods the dye migrated into the nine peripheral ganglia, then through

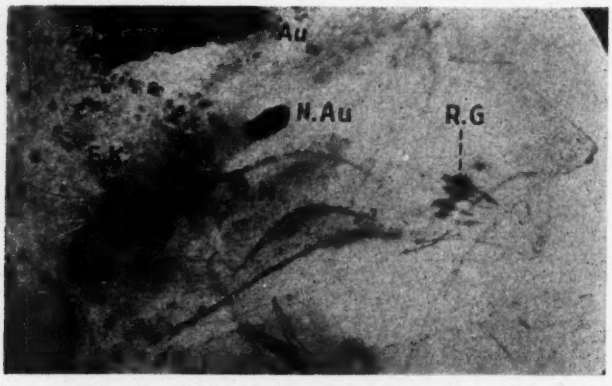

FIG. 4. Elective vital staining of the taste organ of daphnia magna. RN, olfactory nerve, EK, end basket, RG, ganglion, AU, eye, N.AU, naupilus eye.

FIG. 5. Elective vital staining of the taste center of daphnia magna.

the axons into the central ganglia (Schlundganglion). The "Schlundganglion" contains forty-two cells, of which only nine, those belonging to the peripheral rhinosphere rods, became colored by methylene blue. (Figs. 4 and 5.) The stained rhinophore ganglia are in the midst of the other thirty-three ganglia which were not influenced by this staining at all.

This distribution of methylene blue, according to our experience, reveals that a positive charge exists in the central ganglia against the peripheral ganglia and nerve fibers. The peripheral ganglia and nerve fibers are positive without any doubt, however, in relation to their surrounding medium. The potential of this charge was estimated by Gasser[14] on the basis of the electrolyte distribution. (Table VI.) According to the electrolyte distribution the potassium concentra-

TABLE VI

PROBABLE ELECTROLYTE DISTRIBUTION IN THE FROG NERVE

(Concentration in millimolls per cent)

	Inside Axon	Outside Axon
Potassium	17.6	0.27
Sodium	3.7	10.8
Calcium	0.96	0.21
Magnesium	2.4	0.34

tion at the interior is sixty-five times that at the exterior, which would permit a potential of 118 millivolts.

Gerard's[16] analyses supply good evidence for the relative electropositivity of the brain against the peripheral nerves. According to him the brain of mammals contains one and a half or two times as much potassium as the peripheral nerves, and correspondingly less sodium. The brain, however, is full of axons with less potassium and more sodium and also contains numerous blood capillaries with a Na:K ratio of 30:1. Thus an average content of twice as much potassium for the whole brain means in reality a multiple of this figure for the pure ganglion cells.

During stimulation the potassium content of the nerves diminishes in a way similar to that of muscle. Advanced age and disease seem also to have a similar influence according to Petrunkin and Petrunkin,[36] who analyzed the brains of healthy persons killed by accidents. They found more potassium and less sodium in the brains of young and healthy persons than in those of old or sick persons. (Table VII.)

TABLE VII

K, Na AND Cl CONTENT OF BRAINS

	K	Na	Cl
18 years (normal)	4.19	0.94	1.31
60 years (normal)	3.60	1.10	2.07
Tuberculosis	3.63	1.36	1.50
Pneumonia	4.01	1.53	1.86
Nephrosclerosis (62 years)	3.90	1.34	1.85
Cancer	3.83	1.41	1.68

It seems on the whole that the parenchyma of all organs suffers losses of the potassium group and makes gains in the sodium group and water during fatigue. Eppinger,[6] Siedeck and Zuckerkandl[43] found more Na than Cl in the morning urine and less in the evening urine. Nonnenbruch[32] came to the conclusion after the observation

of healthy and sick persons, that water is retained in fatigue and is released after rest.

THE ELECTRICAL POTENTIAL OF THE KIDNEY AS A FACTOR IN ITS FUNCTION

In most glandular organs the investigation is concerned with the part that their secretion plays in the various phases of the metabolic processes. The investigators of kidney function, however, are confronted with a problem of more fundamental nature. This is due to the fact that aside from the formation of hippuric acid and ammonia, no chemical transformation occurs in the kidney; the main product of kidney function, the urine, being excreted, plays no further rôle in metabolism. The question here is, how is urine produced from the blood plasma? Therefore it revolves around the problem of the manner in which the cells themselves carry out their work.

The fundamental nature of the problem explains the slow progress made in spite of the large amount of work done. But this very fundamental quality means that progress in kidney research will elucidate not only organ but cell function in general, and success in investigation on the kidney will help to advance research in the activity of living protoplasm. Because we are considering cell function in general and because the interpretation of the findings is based on electrical phenomena, which are explained by showing examples in other glands, one cannot discuss the activity of the kidney without considering other organs and comparing their function with that of the kidney. Comparison of the different types of kidneys in various animals is also of interest and the results are striking, because the micro-electrical properties of the kidney in the vertebrate and of the nephridia in invertebrates are nearly identical, although morphologically these organs are dissimilar.

Experiments with fluorescent dyes have given important clues to the electrical charge of the various cells of the kidney. Singer has shown that the components of the glomerular loops can be selectively stained and on the basis of this staining the different components of the Malpighian body can be delineated according to their electrical properties. The two typical pictures shown here (Figs. 6 and 7) demonstrate how entirely dissimilar is the appearance of the same Malpighian body according to the characteristics of the dye applied. A cathodic substance (acid, positively charged esculine) was applied in the first case, and an anodic substance (alkaline, negatively charged acriflavine) in the second case. The positively charged escu-

line stained the capillary wall, the negatively charged acriflavine stained the glomerular epithelium.

As the presence of fluorescent dyes is detectable in very minute

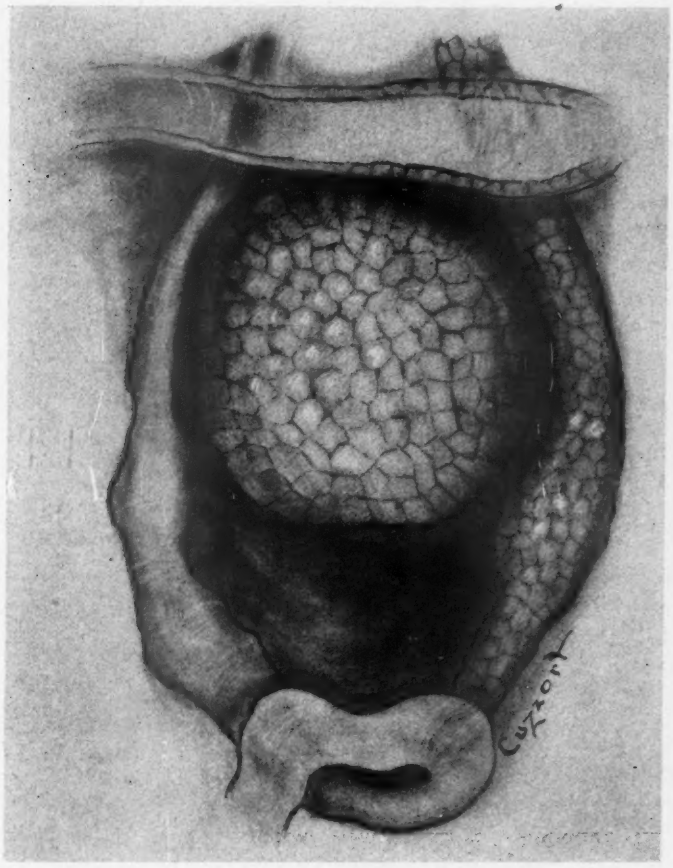

FIG. 6. Glomerulus in fluorescent light of acriflavine.

quantities, the migration of the dyes could be observed. This is especially the case in Singer's[45] double fluorochroming process, when one positively and subsequently one negatively charged substance are applied to produce fluorescence. By this method one can see clearly how the negatively charged dye passes through the negatively charged cytoplasm on its way to the positively charged nucleus, where it becomes concentrated and stored for a longer time. Special consideration should be given to this fact. By not taking this migration into consideration an erroneous interpretation was given in one of Singer's earlier papers, where it is stated that acriflavine, a negatively charged dye, stains the cytoplasm of the cells.

The speed of the migration appears to be influenced by the electrical charge. From the various substances Singer examined, the

fluorescence of the acid ones (which have a positive charge in the blood plasma) appeared almost instantaneously in the glomerular capsule. The fluorescence of the alkaline substances with similar

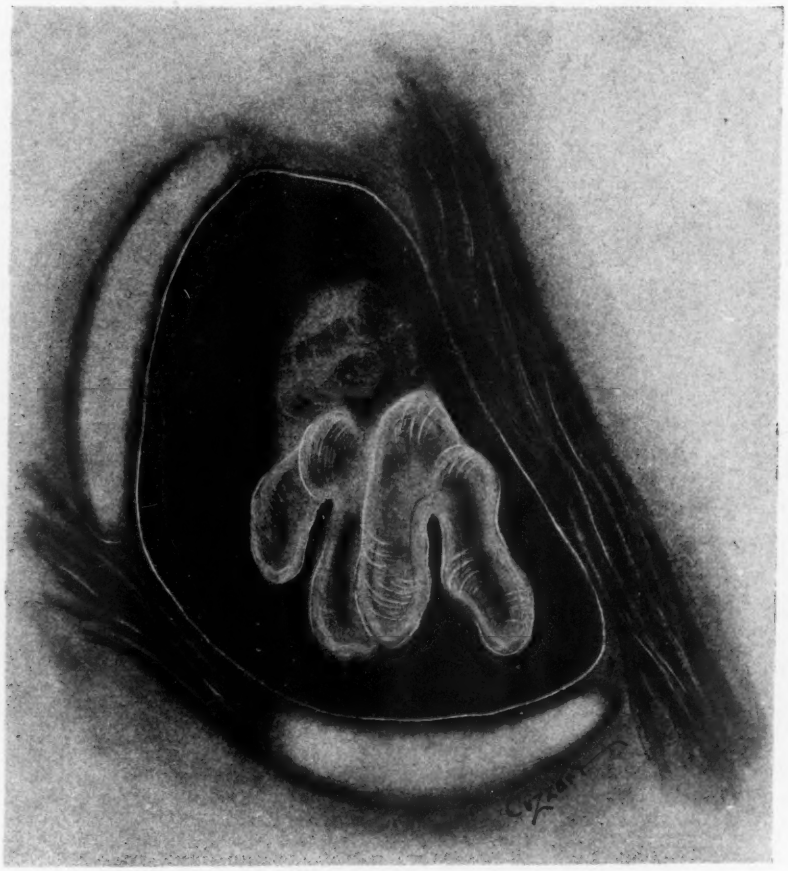

FIG. 7. Glomerulus in fluorescent light of esculine.

colloid dispersion (which have a negative charge in the blood plasma) appeared much later in the capsule and never attained a high intensity in it. Although the appearance of fluorescence is not sufficient for quantitative estimation, since the findings are similar to Fischer's[9] observations on the aqueous humor it would indicate that the mechanism of these seemingly basically different physiologic functions, the glomerular filtration and humor formation, might be the same.

It was observed by Singer, that substances with opposite charge penetrate from the lumen of the tubule into the same cells. The various substances, however, migrated to different parts of the cells. Thus the fluorescent staining of the tubules showed clearly that the cytoplasm of the cells which form the wall of the tubules is

not a homogeneous positive or negative mass. It was seen that the lack of homogeneity is caused by granuli; and the staining experiments with fluorescent substances and with dyes visible in ordinary

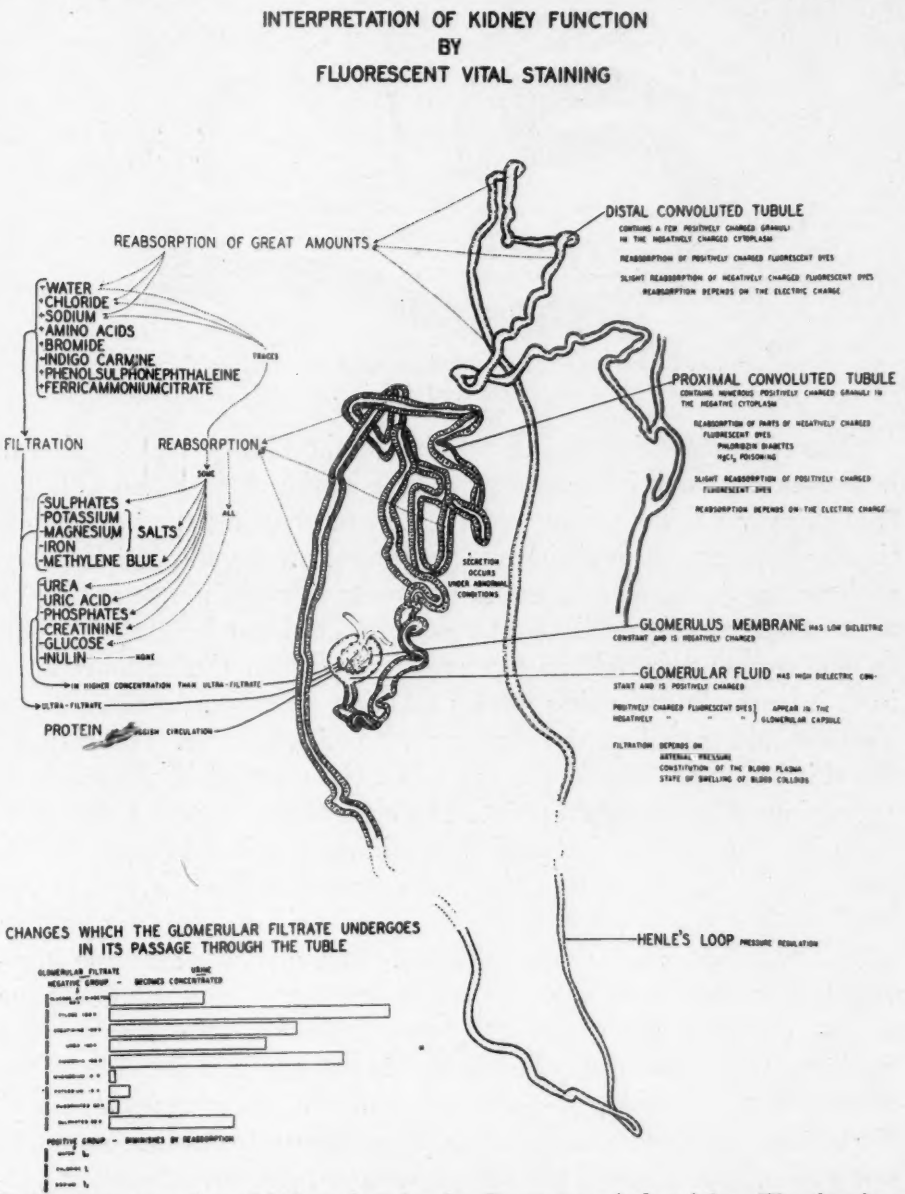

FIG. 8. Interpretation of kidney function by fluorescent vital staining. The drawing is a semi-diagrammatic representation of a nephron dissected by Dr. Jean R. Oliver.

light revealed that the proximal convolutions of the tubules consisted of cells having numerous positively charged granuli. The number of the latter gradually decreased so that the distal convolutions contained hardly any. These electrical characteristics of the

kidney cells are in agreement with their functional characteristics as based on microchemical investigations of Richards[37] and his co-workers. (Fig. 8.)

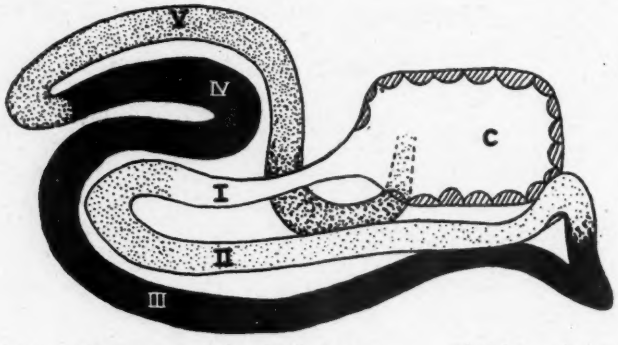

FIG. 9. Segments of the daphnia magna nephridium delineated by vital staining.

The representation of the activity of the kidney cells as shown in Figure 8 (which is based on findings in the mammalian kidney) is strikingly similar to that of Gicklhorn, showing the activity of the daphnia magna nephridium. By the selectivity of vital staining with urotropin-alizarin he could delineate five distinct segments of the nephridial loops. The first segment could not be stained. The second segment stored the dye selectively when the animals were kept in a medium having strong alkaline reaction. In alkaline or electro-positive milieu the dye is relatively negative. The cells of the third segment stored the dye when the reaction of the medium approximated the neutral point. The cells of the loop or fourth segment became stained first and the staining was in this segment the most intensive. The cells of the fifth segment stained only when the medium had a strong acid reaction. In acid or electro-negative milieu the dye is relatively positive. (Fig. 9.) This example illustrates that when working with amphoteric substances a knowledge of the physical and chemical characteristics of the surrounding medium, that is the dispersion phase, is essential. Evaluation of the results of the staining experiments and correct interpretation of the findings can be accomplished only by taking into consideration the influence of the dispersion phase upon the behavior of colloid particles. As the electrical charge of dyes and that of colorless substances depend not only upon the dispersion phase, but upon the concentration, size of particles, and upon other circumstances previously discussed, it is possible that a substance may reverse the direction of its migration. It is of importance to note also that substances with photodynamic action will completely change their behavior after

a short period of illumination (Singer). The changes caused by these influences in the behavior of the substances might explain several contradictory findings of various authors.

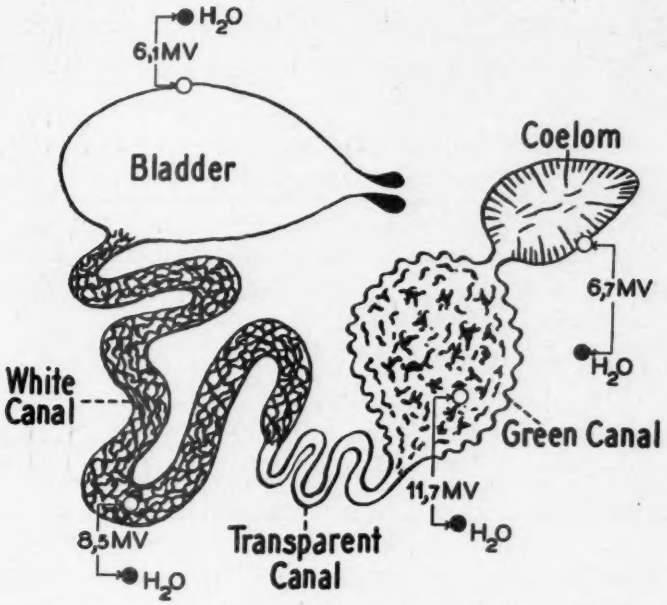

FIG. 10. Schematic picture of the crayfish nephridium showing the electrical potential of its various parts as obtained by microelectrical measurements.

Although one can fit into a general scheme the positively charged substances on one hand and the negatively charged substances on the other, an explanation of reabsorption in the kidney, especially in the proximal convoluted tubules, cannot be based on a simple theory of electrical attraction or repulsion. Quantitative analyses show that the reabsorption is a selective process. To mention one example, all glucose is reabsorbed, but urea is reabsorbed only in part. (Co-workers of Richards[37] found urea crystals in the cells after injection of urea into the tubule as the only evidence of urea reabsorption.) Conceding that glucose is much more negative than urea, as Keller's measurements in high tension apparatus showed, still one cannot neglect the fact that adsorption, chemical reactions, and various other circumstances might play a rôle in the selective activity of the tubular cells.

Potential measurements with micro-electrodes made by Gicklhorn[17] on crayfish nephridium showed a varying negativity of the cells, but also showed that the highest negative potential coincided with the segment in which vital staining was most intensive. This

segment is also the site of the most intensive water reabsorption. The numerical values are shown in Figure 10.

The electrical potentials found by vital staining and by measurements with micro-electrodes are in harmony with the findings on the mineral contents of the kidney. Fischer[9] gives the numerical values as shown in Table VIII. The antagonistic electric groups are

TABLE VIII
ASH CONTENT OF KIDNEY
(Average values in mg. per cent)

	Cl	Na	Ca	P_2O_5	SO_4	K	Mg
	+	+	+	−	−(?)	−	−
Cortex	149	171	12	450	264	411	20
	179	205	13	328	206	422	20
	185	217	14	357	227	410	19
	284	270	22	192	402	304	4
Medulla	402	347	22	199	429	337	5
	398	359	25	194	470	325	5

distributed according to their electrical charge. The cortex, where the positive structures prevail, contains the potassium group; the medulla, where the negative structures prevail, contains the sodium group. Consequently we meet again with the same group distribution of biologically positive and negative substances as we have seen in other organs.

If one compares the amount of the positive and negative groups in the glomerular filtrate and in the urine, one sees that the positive group becomes diluted and the negative group becomes concentrated. (Figure 8.) Sodium is reduced in the distal convoluted tubule to one-twelfth of the amount found in the glomerular filtrate, chloride to one-eleventh, and water to one-fiftieth. The concentration of SO_4 is increased eighty times; that of P_2O_5 six times, K fifteen times, Mg four times, NH_4 150 times (this compound is produced partly by the kidney itself), urea 100 times, creatinine 120 times, xylose 180 times, and glucose in various forms of glycosuria sixty times. Similar changes occur in the concentration of these two groups in the secretion of several other glandular organs.

A comparison between the bile in the hepatic ducts and that in the gall-bladder reveals that the positively charged water is reduced to one-seventh and sodium to about one-third of their previous amounts. The negatively charged mucine and pigments are concentrated eight times, taurocholate nine times, glycocholate eleven

times, fatty acids nine times, bilirubin seventy-eight times. The difference in the concentration of these two groups is less marked between the two types of bile than between glomerular filtrate and urine. One has to take into consideration, however, the fact that the bile in the hepatic ducts is already concentrated by reabsorption of water and chlorine. Comparison between bile in the bile capillaries and that in gall-bladder would show a closer resemblance to the conditions found in the kidney. It is, however, technically extremely difficult to obtain pure bile from the bile capillaries. Keller, in unpublished experiments, succeeded in obtaining pure capillary bile from rabbits; the figures of five experiments show that capillary bile contained respectively 16, 3, 7, 0, and 17 mg. per cent more sodium chloride than bile in the hepatic ducts. Thus the biliary ducts which show identical electrical properties to the distal convoluted tubules of the kidney perform a similar function.

A comparison between milk and blood plasma shows a similar dilution and concentration of the positively and negatively charged substances in the mammary gland. In unpublished experiments, Keller found similar grouping in the distal parts of the ducts in salivary glands, in sweat glands, and in the glands of the intestines. Data collected from the literature show that in most cases free acid wanders in a similar direction with the strong base potassium and the weaker base magnesium or methylene blue. (Table IX.) Exceptions to this rule are found mostly in plant cells (Osterhout[35]).

TABLE IX

POTASSIUM-SODIUM RATIO AND *pH* IN BIOLOGICALLY ELECTRO-NEGATIVE PLACES

(Blood serum K/Na ratio 1:20, *pH* 7.4)

	K/Na Ratio	*pH*
The three salivary glands (Babkin[1])	14:1	6.63
Fundus glands in stomach (Rosemann[39])	2:1	0.88
Sweat glands	2:1	6.90
Mammary gland (cow)	3:1	6.50
Urine (herbivorous animals)	10:1	6.50
IN BIOLOGICALLY ELECTRO-POSITIVE PLACES		
Pylorus glands in stomach	1:4	8.50
Pancreas secretion	1:14	8.6

The analysis of the secretions of glands enumerated in Table IX shows that they are the results of a shifting of the contrasting electrical groups as in the urine. The ducts of these glands consist of electrocytologic structures similar to the distal convoluted tubules

of the kidney. With the similar electrical property goes a similar function. All the glands mentioned reabsorb in their ducts the electro-positive water and sodium chloride and amino acids from the secret fluid in their lumen and by this they concentrate the electro-negative contents of the secretions. Due to the length of the distal convoluted tubules of the kidney the concentration effected by them is higher than that produced by other glands. Thus the function of the distal convoluted tubules of the kidney can be explained by their micro-electrical structure and it can be shown that this function is characteristic of other structures with similar electrical properties. The complicated structure and function of the proximal convoluted tubules, however, cannot be elucidated this way.

THE SOURCE OF ELECTRICAL POTENTIAL

Lund[28] and his co-workers found that those tissues which have the strongest respiration produce the highest electrical potentials. According to Eppinger[6] and his co-workers, lack of oxygen depresses not only the electrical potential of the liver, but also that of the heart, the cross-striated muscles, and the kidney. Kaunitz[19] analyzed the hearts of sixty guinea pigs and found that eighteen were normal, nineteen were under the effect of lack of oxygen, and twenty-three were under the effect of various poisons. In the two latter groups he found heavy losses of potassium in the heart tissue. Due to the effect of lack of oxygen the potassium content declined from 227 to 357 mg. per cent to 153 to 293 mg. per cent. Poisoning with diphtheria toxin, he found, produced a potassium content of 175 mg. per cent, Mg poisoning 143 mg. per cent, and urea poisoning 156 mg. per cent. Kaunitz proved by this that with a definite electrical potential of the tissues goes a certain content of minerals characteristic of that potential.

While several processes thus *depress* the electrical potential of tissues against blood, numerous other processes may *increase* this tension even above normal. Among the chemical compounds which have this effect are digitalis, strophanthin, ascorbic acid (this only in extremely large quantities), quinine, amidopyrine, and novalgine. This phenomenon of increased tension is accompanied by abnormally high potassium content of the liver, heart and muscles. Potassium content of the heart after digitalis increased, according to Kaunitz, to 361 mg. per cent, after novalgine to 326, 317, and 334 mg. per cent.

Some other occurrences observed by other authors should be classified here. Matsuo,[30] who conducted a great number of experiments on vital staining in man and animals, found that patients

during convalescence and experimental animals during the recovery period from various damaging effects showed stronger staining than healthy ones. Keller found, in unpublished experiments on transparent animals (daphnia, cyclops, and paramecium), that vital staining is weak in sick animals and in animals with oxygen deficiency. He also found that vital staining is weak after the application of ammonium salts, whereas the intensity of vital staining increased in these animals after application of quinine, pyrazolon, and various other phenol derivatives. Osterhout,[35] Blinks,[2] and co-workers depressed or increased the electrical potentials of plants according to whether they applied ammonium chloride and oxygen deficiency or various phenol compounds.

Our experiments and the experiments of the above-mentioned authors, especially those of Lund and his co-workers, support the idea that at least part of the energy necessary for the metabolic processes is produced by the electrical potential difference of the positive carbon and hydrogen on one side and the negative oxygen on the other side.

The variation of potassium content in muscle, heart, and liver as shown by Kaunitz indicates that the positive potential of these organs against blood is reduced by oxygen deficiency, by fatigue and by certain poisons; and is increased by digitalis and the pyrazolon group.

It seems plausible that the energy necessary to some phase of the metabolic activity derives from electrical forces. Other sources supply energy to other phases of the metabolic activity. To illustrate this, let us take the liver and muscle as an example.

On the basis of evidence presented we can accept that during the digestion phase the electric current fills the storage places in the liver and muscle. In normal human beings under ordinary conditions this occurs up to midnight. After this time from 1 or 2 o'clock A.M., according to Forsgren's observations,[10] the liver gives back a great part of its glycogen to the circulation. It can be accepted, we think, as a probability, that the electrical potentials are diminishing in these hours, and the osmotic pressure of the high carbohydrate concentration in the liver becomes stronger than the electrical counter-force and about 200 Gm. of carbohydrate from the liver, perhaps some also from the muscle stores, return to the serum against the electrical force by diffusion force. It seems plausible that the same counteracting forces might be responsible for the occurrences caused by fatigue, by the effect of toxins, and by oxygen deficiency, and for the other conditions mentioned.

Up to this point we have discussed the way in which the study of chemical changes gives us a key for the understanding of electrical phenomena. There is, however, at least one electrical phenomenon

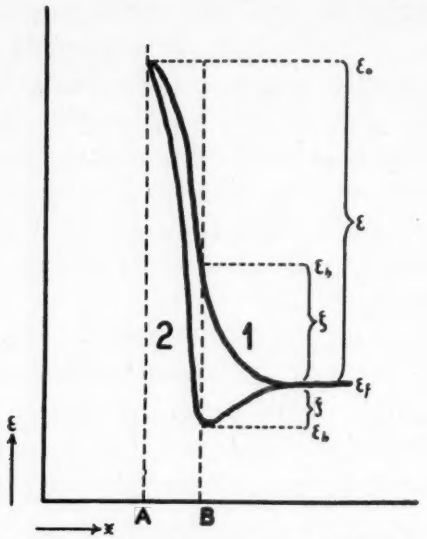

FIG. 11. Potential difference on the border line of a solid wall against the fluid. ϵ, the difference in potential between the solid wall against the movable fluid. ζ, the difference in potential of the fluid adherent to the solid wall against the inside movable fluid. A, the solid wall; B, the movable fluid. Abscissa is the distance of a given point from the wall; ordinates represent the potentials.

in the organism that finds the key to its explanation in a physical process only. This is the contact potential or "Phasengrenzkraft" (Freundlich[11]).

The potential difference that arises when two substances come in contact was observed by Coehn[4] in 1899. He formulated a rule that governs the origin of this potential: A substance having a higher dielectric constant coming in contact with a substance of lower dielectric constant becomes positively charged against the latter. On the borderline of two phases we deal with this type of potential. (Fig. 11.) Part of the static positive charge of the lymph, aqueous humor, and the glomerular filtrate results from this source. This rule of Coehn might be also the explanation for the findings that the glomerulus through which the water is forced by hydrodynamic pressure and the iris of the eye in which the same thing occurs, are, when alive, negatively charged, but lose their negativity after cessation of the blood pressure.

THE MIGRATION OF MINERALS BETWEEN PLASMA AND RED BLOOD CORPUSCLES AND BETWEEN PLASMA AND PARENCHYMATOUS ORGANS DUE TO THE EFFECT OF DISEASE UPON ELECTRICAL POTENTIALS

In the previous paragraphs it was pointed out that the electrical potentials of organs vary with their functional state. Numerous experiments of our own and those collected from the literature were

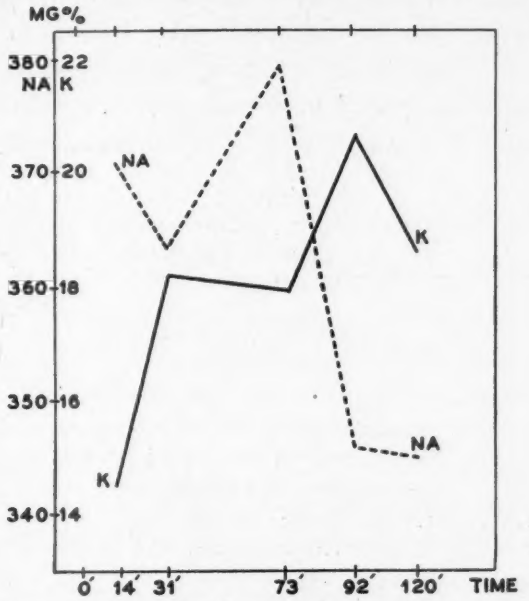

FIG. 12. The migration of sodium and potassium between blood corpuscles and serum during the necrosis of the blood corpuscles in vitro.

cited to support and prove this contention. Reference was made also to the fact that the functional derangements occurring in various diseases affect the electrical potential and cause a shifting in the positively and negatively charged substances.

The shifting of the mineral groups is most characteristic in severe diseases. Waelsch, Kittel and Busztin[55] made several thousand blood corpuscle and plasma analyses in healthy and in sick individuals. These analyses showed that sodium wandered in places to displace potassium and potassium wandered in places to displace sodium. Displacement of minerals occurs also in vitro between serum and blood corpuscle. The manner in which this occurs was studied by these investigators and they found that the equilibrium between these two groups is not a result of a straight progress line, but is subjected to strong fluctuations. The magnitude of the fluctuation peaks is only slightly dependent on the temperature, while the direction of the fluctuation is entirely independent of the tempera-

ture. Figure 12 shows a typical curve of the development of the equilibrium. It is possible that these fluctuations are due to fluctuations in potential difference between red blood corpuscles and plasma that occur during the necrosis of the blood corpuscles. On the basis of this analysis it seems justifiable to consider that the composition of the serum is a result of a mineral exchange between blood corpuscles and plasma which occurs during the clotting process. The composition of plasma in the circulating blood, which would be most important for our interpretation, can only be tentatively estimated. Schmitt's analyses[41] approach the true values closely, because she was able to separate blood corpuscles and plasma by a very

TABLE X

MIGRATION OF MINERALS BETWEEN PLASMA AND RED BLOOD CORPUSCLES

(Values in mg. per cent)

Diagnosis	Plasma			Red blood Corpuscle			Change in Disease					
							Plasma			Red Blood Corpuscle		
	Cl	Na	K	Cl	Na	K	Cl	Na	K	Cl	Na	K
Normal	364.5	310	20.5	254	152	303	0	0	0	0	0	0
Diabetic coma	318	282	21.9	323	134	274	−46	− 28	+ 1.4	+ 69	−18	− 29
Diabetic precoma	315	279	23.3	342	139	266	−49	− 31	+ 2.8	+ 88	−14	− 37
Nephritis with low plasma Cl	307	268	34	324	159	232	−57	− 42	+13.5	+ 70	+ 7	− 71
Chronic nephritis with high plasma Cl	371	309	34	327	160	320	+ 7	− 1	+13.5	+ 73	+ 8	+ 7
Hypochloremia (gastric ulcer)	281	300	27.9	102	62	265	−83	− 10	+ 7.4	−152	−90	− 38
Carcinoma of stomach (inoperable)	365	256	40	131	92	262	+ 1	− 54	+19.5	+ 23	−60	− 41
Carcinoma of stomach (operable)	364	280	38	202	74	281	0	− 30	+17.5	− 52	−78	− 22
Polyserositis carcinomatosa	349	151	45	147	68	411	−15	−159	+24.5	− 7	−84	+108

rapid method. Table x is calculated therefore on the basis of her findings. It shows a displacement in potassium and sodium content of the blood corpuscles and serum similar to that observed by Waelsch.

Uher[53] examined livers of patients who died from a variety of causes, such as phthisis, general sepsis, pernicious anemia, carcinoma, intoxication, peritonitis, diphtheria, diabetes, and cardiac diseases. The graphs based on his findings show that potassium and sodium change places as in the blood plasma, that is, they wander in

opposite directions to each other. The conditions found in the serum, therefore, reflect the condition of the entire organism. Waelsch found that in severe illness the storage places for the negatively charged substances lose their stored material because the decreased positive electrical charge is not able to retain the full amount and the decreased negative charge of the serum does not repel it. Thus serious illnesses are characterized by a tendency to level the electrical charge and to even the distribution of the antagonistic chemical groups. Waelsch calls this the electrical and chemical dedifferentiation of the organism.

CONCLUSIONS

We have attempted to show in this paper by evidence based on the findings of our own experiments and on data collected from the literature, that lithium, sodium, part of chlorine, part of calcium, and part of magnesium seem to be ionized in living cells. Other substances form non-dissociated macro-molecules in living cells. The charge of these macro-molecules has to be determined experimentally in each case. Thus we cannot divide the radicals of acids and bases into anions or cations, as is possible in distilled water. The division of substances into positively charged and negatively charged groups has to be made according to their behavior in the electric field of biocolloids.

The thin surface membranes or layers of the living protoplasm are able to exert attraction and repulsion forces for both groups and are able to move them in opposite directions. The substances move in the living protoplasm according to their electrical charge. The electrical charge of the various substances as it exists in the living protoplasm, that is in a medium which is rich in colloids, is the decisive factor for their migration. The theoretical electrical charge that one finds with perfectly dissociated salts in distilled water has no bearing upon the behavior of the various substances in living medium. The *p*H of the various substances as long as they are in physiologic dilutions is of secondary importance to the living cell.

The electrical behavior of living cells plays an important rôle in metabolism and reflects the physiologic or pathologic condition of the organism.

If one acquaints himself with the fact that one has to differentiate between a small group of non-complex-forming substances, that is substances really ionized (dissociated) in living cells, and another large group of complex-forming substances including many minerals, which when greatly diluted in living cells always behave as negatively

charged (anodic) macro-molecules, then one is able to find the confusing mineral tables of the organs readable and comprehensible. The explanation of a great number of physiologic and pathologic processes becomes greatly facilitated by the study of electrical phenomena in microscopic dimensions.

SUMMARY

1. The surface potentials of various substances play an important rôle in cell metabolism.

2. The electrokinetic potential or ζ potential (Freundlich) is of universal importance in life processes. The contact potential (Phasengrenzkraft) plays a more limited rôle.

3. The electrical potentials of organs vary with their functional state.

4. Pyrazolon, digitalis, strophanthin, and natural convalescence show a tendency to raise the electrical potentials to a normal level. Various phenol derivatives raise the electrical potential above the normal level. Narcotics and ammonium salts decrease the potential.

5. Qualitative estimation of the electrical charge can be made by vital stainings. Quantitative measurements have to be made by non-polarizing micro-electrodes.

6. There are two groups of substances; one group is attracted where the positive electrical potential exists, the other group where the charge is negative.

7. The organism contains the two groups according to its electrical potential in its various organs.

8. The electrical groups in living cells which are rich in colloids, have an electrical charge, which has to be found by experiments and must not be confounded with their charge as ions in dissociation in distilled water.

9. In most diseases, in fatigue, in oxygen deficiency, and under the influence of many poisons, the K group (negative group) goes out of the cells and the Na group (positive group) enters into them.

10. The liver is an organ of high positive potential in its parenchymal and reticulo-endothelial cells, and has a high negative potential in its bile capillaries. The blood capillaries and connective tissue in the liver have electrical potentials that are identical with the electrical potentials of these tissues in other organs.

11. Blood corpuscles (positive) and blood serum (negative) have contrasting electrical charges which become depressed in pathologic processes.

12. The secretion of glands derives from the blood serum and lymph. These fluids are rich in NaCl and poor in K. Glands, however, secrete a K-rich and NaCl-poor fluid. This is due to reabsorption of NaCl and water in the distal tubules of the glands. The concentration in the K group is due to the reabsorption of the other constituents of the preliminary gland secrets.

REFERENCES

1. Babkin, B. P. Die äussere Sekretion der Verdauungsdrüsen. Berlin, 1928.
2. Blinks, L. R. *J. Gen. Physiol.*, 20: 00, 1936–1937.
3. Chambers, R. *J. Gen. Physiol.*, 5: 189, 1922–1923.
4. Coehn. *Wied. Ann.*, 64, 1898.
5. Dejdar. In Schornstein. *Protoplasma*, 19: 41, 1933.
6. Eppinger, Kaunitz and Popper. Die seröse Entzündung. Vienna, 1931.
7. Fenn, W. O. *Cold Spring Harbor Symposium*, 4: 252, 1936.
8. Fischer, F. P. *Kolloid. Beihefl.*, 28: 333, 1929.
9. Fischer, F. P. *Biochem. Ztschr.*, 268: 336, 1934.
10. Forsgen, E. Über die Rhythmik der Leberfunktion. Stockholm, 1935.
11. Freundlich, H. Kapillarchemie. Leipzig, 1922.
12. Fürth, R. *Ztschr. f. Physiol.*, 68: 735, 1931.
13. Gamble. *J. Biol. Chem.*, 57: 633, 1923.
14. Gasser, H., Erlanger, J., and Gasser, H. Electrical Signs of Nervous Activity. Philadelphia, 1937. University of Pennsylvania Press.
15. Gelfan, S. *Proc. Soc. Exper. Biol. & Med.*, 29: 58, 1931.
16. Gerard, W. R. *Cold Spring Harbor Symposium*, 1936.
17. Gicklhorn, J. *Zool. Anz.*, 67: 257, 1935.
18. Irwin, M. J. *J. Gen. Physiol.*, 8: 147, 1925; 12: 407, 1928–1929.
19. Kaunitz, H. *Ztschr. f. klin. Med.*, 131: 192, 1937.
20. Kaunitz, H., and Schober, B. *Ztschr. f. klin. Med.*, 131: 219, 1937.
21. Keller, R. Die Elektrizität in der Zelle. Märisch-Ostrau, 1933.
22. Keller, R. *Folia hemat.*, 52: 283, 1931.
23. Keller, R., and Gicklhorn, F. *J. Psych. & Neurol.*, 32: 64, 1925.
24. Kreibich. Personal communication.
25. Lamb. *Brit. A. Rep.*, 1882.
26. Lillie, R. S. Protoplasmatic Action and Nervous Action. Chicago, 1923. University of Chicago Press.
27. Loeb, J. *Biochem. Ztschr.*, 31: 450, 1911.
28. Lund, E. J. *Plant Physiol.*, 6: 631, 1931.
29. Marsh, G. *J. Exper. Zool.*, 51: 309, 1928.
30. Matsuo, I. Biologische Untersuchungen über Farbstoffe. Kyoto, 1934.
31. Nistler, L. Mikroelektrische Untersuchungen am Verdaungskanal. Märisch-Ostrau, 1933.
32. Nonnenbruch, W. *Deutsch. Arch. f. klin Med.*, 136: 170, 1921.
33. Okuyama. *J. Biochem.*, 14: 69, 1931.
34. Osterhout, W. J. V. *Kolloid. Ztschr.*, 77: 373, 1936.
35. Osterhout, W. J. V. *J. Gen. Physiol.*, 18: 987, 1935.
36. Petrunkin and Petrunkin. *J. Physiol. & Path.*, 33: 1103, 1935.
37. Richards, A. N. *J. Biol. Chem.*, 101: 179, 1933.
38. Roller and Schober. *Ztschr. f. exper. Med.*, 10: 551, 1936.
39. Rosemann. *Pflüger's Arch.*, 118: 467, 1907.
40. Rosene, H. F., and Lund, E. J. *Plant Physiol.*, 10: 27, 1935.
41. Schmitt, Naunyn and Schmiedeberg. *Arch.*, 181: 562, 575, 581, 1936.

42. SEKI, M. *Okayama-Igakki Zassbi*, 372, 1921; *Ztscbr. Zellforscb.*, 17: 138, 1933.
43. SIEDECK and ZUCKERKANDL. *Klin. Wcbnscbr.*, 567: 1137, 1428, 1935.
44. SINGER, E. *Anat. Rec.*, 53: 37, 1933.
45. SINGER, E. *Am. J. Anat.*, 53: 469, 1933.
46. SINGER, E. *Anat. Rec.*, 58: 38, 1934.
47. SINGER, E. *Anat. Rec.*, 60: 183, 1934.
48. SINGER, E. *Anat. Rec.*, 64: 44, 1936.
49. SINGER, E. *Anat. Rec.*, 66: 343, 1936.
50. SINGER, E. *Arcb. Patb.*, 22: 813, 1936.
51. SINGER, E. *Am. J. Anat.*, 53: 464, 1933.
52. TISDALL, F. J. *J. Biol. Cbem.*, 57: 633, 1923.
53. UHER, V. *Ztscbr. f. exper. Med.*, 96: 159, 1933.
54. UNNA. Abderhalden's Handbuch, Abt. 5, T. 2, 1921.
55. WAELSCH, H. S., KITTEL, A., BUSZTIN, HOPPE-ZEILLER. *Ztscbr. f. physiol. Cbem.*, 234: 1, 1934.
56. WERTHEIMER. *Pflüger's Arcb.*, 200: 354, 1923; 206: 165, 1924; 208: 669, 1925.